

Document made available under the Patent Cooperation Treaty (PCT)

International application number: PCT/EP04/013539

International filing date: 29 November 2004 (29.11.2004)

Document type: Certified copy of priority document

Document details: Country/Office: EP
Number: 04001894.7
Filing date: 29 January 2004 (29.01.2004)

Date of receipt at the International Bureau: 18 January 2005 (18.01.2005)

Remark: Priority document submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b)



World Intellectual Property Organization (WIPO) - Geneva, Switzerland
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Patentanmeldung Nr. Patent application No. Demande de brevet n°

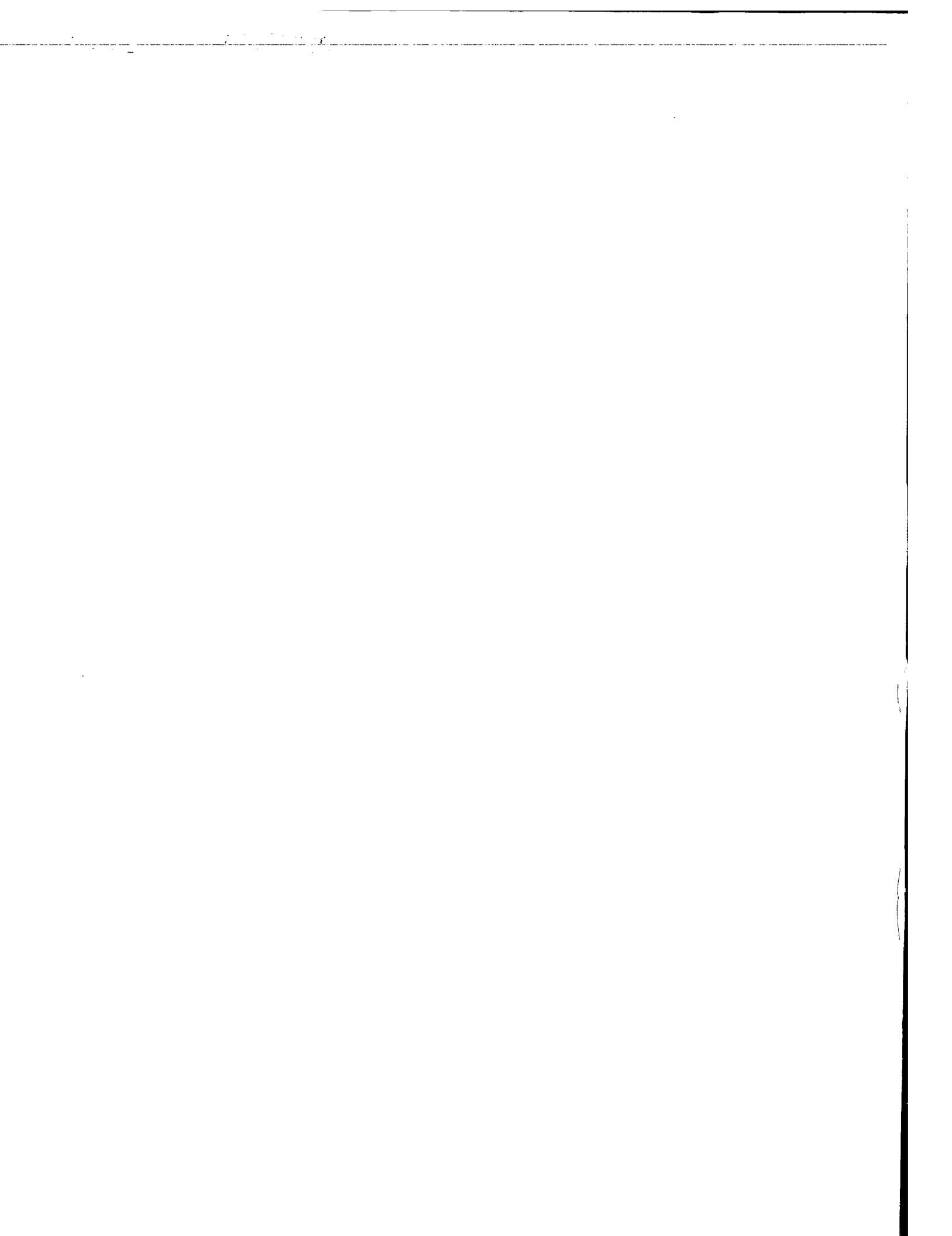
04001894.7

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Im Auftrag

For the President of the European Patent Office

Le Président de l'Office européen des brevets
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R C van Dijk





Anmeldung Nr:
Application no.: 04001894.7
Demande no:

Anmeldetag:
Date of filing: 29.01.04
Date de dépôt:

Anmelder/Applicant(s)/Demandeur(s):

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Bezeichnung der Erfindung/Title of the invention/Titre de l'invention:
(Falls die Bezeichnung der Erfindung nicht angegeben ist, siehe Beschreibung.
If no title is shown please refer to the description.
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Composition of protein complexes associated with beta-amyloid precursor protein processing

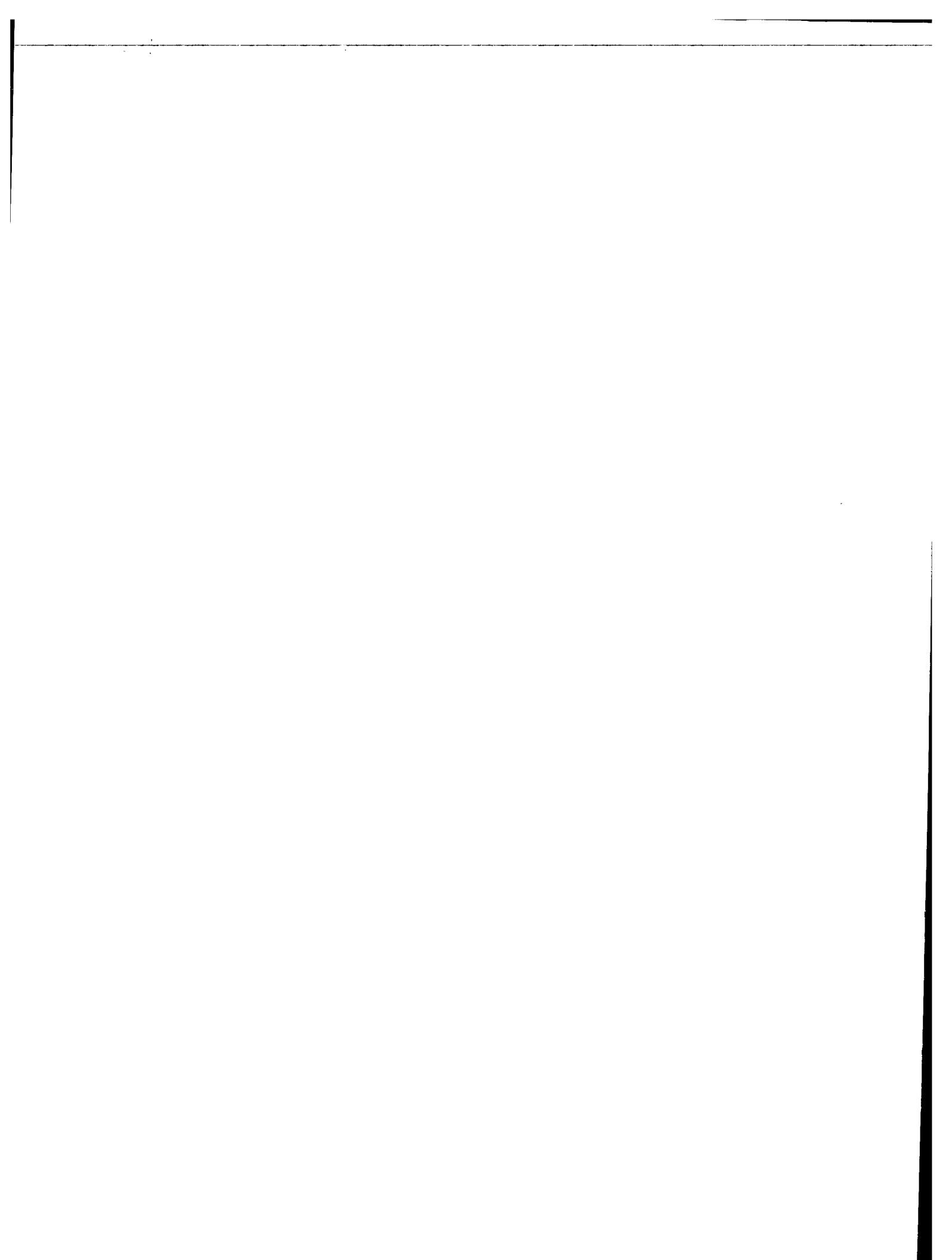
In Anspruch genommene Priorität(en) / Priority(ies) claimed /Priorité(s)
revendiquée(s)
Staat/Tag/Aktenzeichen/State>Date/File no./Pays/Date/Numéro de dépôt:

Internationale Patentklassifikation/International Patent Classification/
Classification internationale des brevets:

C07K/

Am Anmeldetag benannte Vertragstaaten/Contracting states designated at date of
filing/Etats contractants désignées lors du dépôt:

AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU MC NL
PT RO SE SI SK TR LI



29. Jan. 2004

1. FIELD OF THE INVENTION

The present invention relates to protein complexes of the beta-amyloid precursor protein (APP) processing pathway, component proteins of the said complexes, fragments and derivatives of the component proteins, and antibodies specific to the complexes. The present invention also relates to methods for use of the complexes of the APP processing pathway and their interacting proteins in, inter alia, screening, diagnosis, and therapy, as well as to methods of preparing the complexes.

2. BACKGROUND OF THE INVENTION (references are listed in supra)

Alzheimer's disease is a chronic condition that affects millions of individuals worldwide. After onset of the disease sufferers require a high degree of supervision and care. As the proportion of aged individuals in the population increases, the number of sufferers of Alzheimer's disease is expected to expand dramatically. Current top drugs (e.g. Aricept®/donepezil) attempt to achieve a temporary improvement of cognitive functions by inhibiting acetylcholinesterase, which results in increased levels of the neurotransmitter acetylcholine in the brain. These therapies are not suitable for later stages of the disease, they do not treat the underlying disease pathology, and they do not halt disease progression. The growing need for an effective therapy, coupled with the absence of effective treatments, presents a significant opportunity for drug target development and drug discovery.

The brains of sufferers of Alzheimer's disease show a characteristic pathology of prominent neuropathologic lesions, such as the initially intracellular neurofibrillary tangles (NFTs), and the extracellular amyloid-rich senile plaques. These lesions are associated with massive loss of populations of CNS neurons and their progression accompanies the clinical dementia associated with AD. The major component of amyloid plaques is the amyloid beta peptide. Amyloid beta is the proteolytic product of a precursor protein, beta amyloid precursor protein (beta-APP or APP). APP is a type-I trans-membrane protein which is cleaved by several different membrane-associated proteases. The first cleavage of APP occurs extracellularly by one of two proteases, alpha-secretase or beta-secretase. Beta-secretase or BACE1 (beta-site APP-cleaving enzyme) is a type-I transmembrane protein containing an aspartyl protease activity (described in detail below). Alpha secretase is a metalloprotease whose activity is most likely to be provided

by one or a combination of the proteins ADAM10 and ADAM17. Following either the beta or alpha cleavage of APP, the final cleavage event occurs within the membrane and is carried out by a protein complex called gamma secretase. It is the combination of the beta and gamma secretase activities that results in the liberation of the Abeta peptides of 40 and 42 residues (there are also lower levels of other forms) from the APP and ultimately the formation of the amyloid plaques responsible for the pathology of Alzheimer's disease. It is believed that the Abeta-42 peptide is the most critical Abeta species, because it shows the most pronounced neurotoxicity, and can aggregate easily, thus forming a nucleus for the aggregation of other Abeta peptides, such as the Abeta-40 which is typically produced at higher levels than the other species.

The applicant's proprietary proteomics technology (TAP/LC-MS/MS) is particularly successful in the elucidation of membrane protein complexes. These multiprotein complexes form the core of the APP processing pathway and are not amenable to other techniques. Known proteins with an important functional role in APP processing were analysed with The applicant's technology to comprehensively chart the dynamic protein interactions that contribute to Abeta production. Selected novel targets are subsequently validated using cellular or biochemical assays. Moreover, purified multi-protein complexes (e.g. beta- or gamma-secretase) do represent defined functional molecular machines, which are used to evaluate the mechanism of known compounds and for the optimisation of leads.

APP intracellular domain (AICD) (AICD) (APP intracellular domain (AICD) (AICD))

The cytoplasmic tail of APP is liberated into the cytoplasm by gamma-secretase cleavage of either the alpha- or beta-C-terminal transmembrane fragment (1). Cao and Sudhof (2) showed that the cytoplasmic tail of APP forms a complex with the nuclear adaptor protein Fe65 and the histone acetyltransferase TIP60. This complex stimulates transcription via heterologous Gal4 or LexA DNA binding domains, suggesting a function of the APP intracellular domain (AICD) in gene expression, analogous to what has been described for the Notch intracellular domain (3). Recent reports suggest that a complex formed by the APP intracellular domain (AICD) and associated proteins could modify expression of genes that function in inflammation (4) or apoptosis (5). Hence, novel

proteins associated with the cytoplasmic and nuclear complexes of the APP intracellular domain (AICD) that regulate APP intracellular domain (AICD) stability and turnover, nuclear translocation, and its transcriptional function, are potential targets for therapeutic intervention.

BACE2

BACE2 is a glycosylated transmembrane protein of the aspartic protease family, constitutes the only paralog of BACE1, and was mapped to the Down's critical region of human chromosome (6-9). Both endoproteases share similar structural organization including a prodomain, a catalytic domain formed via DTG and DSG active site motifs, a single transmembrane domain, and a short C-terminal tail. BACE2 is expressed at low levels in most human peripheral tissues and at higher levels in colon, kidney, pancreas, placenta, prostate, stomach, and trachea. Human adult and fetal whole brain and most adult brain subregions express very low or undetectable levels of BACE2 mRNA (10). BACE2 has a limited effect on the beta-secretase site but efficiently cleaves the sequences near the alpha-secretase site (11). BACE2 localizes in the endoplasmic reticulum, Golgi, trans-Golgi network, endosomes, and plasma membrane, and its cellular localization patterns depend on the presence of its transmembrane domain. BACE1 knockout mice are viable, possibly due to a redundancy in function with BACE2 (12).

Protein complexes involving BACE2 are of potential therapeutic value in AD therapy. The determination of the nature of the proteins interacting with and potentially regulating BACE1 but not BACE2 will constitute suitable therapeutic targets.

BRI

Familial British dementia (FBD) is a neurodegenerative disease characterised by pathological hallmarks that are strikingly similar to AD, including amyloid fibrils and neurofibrillary tangles (13). However the fibrils in FBD are not formed by amyloid-beta peptides as in AD, but from a unique 4-kD protein subunit, called ABRI, that is encoded by a novel gene, BRI (13). The BRI cDNA encodes a protein of 266 amino acids with a putative single transmembrane-spanning domain between amino acids 52 and 74, indicating that this highly insoluble molecule is a type II integral transmembrane protein

with the C-terminal part being extracellular. A potential N-glycosylation site was identified at asp-170. In the disease, a single base substitution at the stop codon of the BRI gene results in a larger, 277-residue precursor, BRI-L. Release of the 34 carboxy-terminal amino acids from the mutated precursor generates the Abri amyloid subunit. It has been reported that both BRI-L and wild-type BRI were constitutively processed by the proprotein convertase, furin, resulting in the secretion of carboxyl-terminal peptides that encompass all or part of Abri (14).

The protein complex around BRI is of high potential therapeutic interest for AD and related neurodegenerative diseases because BRI pathology leads to very similar downstream pathological effects like tangle formation, and hence could provide molecular links between amyloid formation and intracellular pathways eventually leading to tau phosphorylation and tangle buildup.

Dab1

We have used mouse DAB1 because human Dab1 has not been cloned. Mutation in disabled-1 (Dab1) resemble mutations in reelin (Reln) by causing abnormalities in laminar structures throughout the brain and ataxia in reeler and scrambler mice (15). However, Rehn and Dab1 are distinct in their molecular properties. Rehn is a large extracellular protein secreted in the forebrain and the cerebellum. Dab1 is a cytoplasmic adapter protein that functions in phosphorylation-dependent intracellular signal transduction. It is suggested that Dab1 functions downstream of Rehn in a signaling pathway that controls cell positioning in the developing brain (15). Reelin stimulates tyrosine kinases of the src family by a mechanism involving Dab1 (16). DAB1 has also been reported to interact with APP (17) and with the cytoplasmic tails of LRP and LDL receptor (18). It was shown that Rehn binds directly and specifically to the extracellular domains of VLDLR and ApoER2. Blockade of VLDLR and ApoER2 ligand binding correlated with loss of Reelin-induced Dab1 tyrosine phosphorylation. Mice lacking either Rehn or VLDLR and ApoER2 show an increase in the phosphorylation level of tau proteins suggesting that Rehn acts via Vldlr and ApoER2 to regulate Dab1 tyrosine phosphorylation and tau function in neurons (18). The functional role of the binding of Dab1 to the C-termini of APP, APLP1 and APLP2 has not been elucidated.

The protein complex around DAB1 is of high potential therapeutic interest for AD and related neurodegenerative diseases because it could provide further links of amyloid pathology to downstream tangle pathology, and provide targets for the therapeutic modulation of the intracellular pathways leading to tau phosphorylation, tangle buildup, and neuronal death in AD.

Fe65L2

Fe65 proteins are ligands of the cytoplasmic domain of APP (1). The fe65 gene has two paralogues, Fe65L1 (19) and Fe65L2 (20). Fe65L2 encodes a protein of approx. 50 kDa which is expressed predominantly in brain and testis (21). The three paralogues of the Fe65 protein family share three regions corresponding to the protein-protein interaction domains; the WW domain and the two PTB domains, whereas the remaining sequences are poorly related. Like Fe65, Fe65L1 and Fe65L2 genes encode two different protein isoforms, derived from the alternative splicing of a six nucleotide exon within the N-terminal PTB domain, in the presence or absence of two acidic/basic amino acids. Fe65 proteins have been found to translocate into the nucleus and to prevent the activation of the thymidylate synthase gene promoter induced by the transcription factor CP2 by an unknown mechanism (22).

Fe65L2 is able to interact, both in vitro and in vivo, with the intracellular domain of APP. Fe65 and Fe65L2 interact with APP, APLP1 and APLP2 with different efficiencies (20). Overexpression of Fe65L2 was reported to increase secretion of Abeta 1-40 and Abeta 1-42, however the molecular mechanism of this amyloidogenic effect is unknown. A c954C-->T polymorphism in the Fe65L2 gene is possibly associated with early-onset Alzheimer's disease (21). Fe65 proteins have been found to translocate into the nucleus and to prevent the activation of the thymidylate synthase gene promoter induced by the transcription factor CP2 by an unknown mechanism (22). There are no interactors of Fe65L2 known that are not also found with Fe65.

The protein complex around Fe65L2 is of high potential therapeutic interest for AD and related neurodegenerative diseases because membrane-associated, cytoplasmic and nuclear complexes of the APP intracellular domain (AICD) with adaptor proteins regulate APP stability and turnover, nuclear translocation, and its transcriptional function, which are all potential targets for therapeutic intervention.

Pilt/TJP4

Pilt, also termed TJP4, was cloned as a novel tight junction protein that contains coiled-coils and a proline-rich domain (23). It binds to hDlg. X11 is a negative regulator of Abeta secretion.

Pilt is a novel interactor of X11beta. Novel proteins associated with X11beta and Pilt could regulate APP turnover and processing and APP intracellular domain (AICD) dependent gene expression, and hence are potential targets for therapeutic intervention.

Paladin

Paladin is a novel protein tyrosine phosphatase. The physiological role, subcellular localisation, substrates, and interacting proteins are unknown.

In addition to the predicted PTP domain, there is a second less perfectly conserved PTP domain. Part of other sequence regions are also duplicated. Paladin could bridge dimers of X11 and APP. Paladin is a novel interactor of X11beta and the C-terminus of APP.

Novel proteins associated with X11beta and the C-terminus of APP could regulate APP turnover and processing and APP intracellular domain (AICD) dependent gene expression, and hence are potential targets for therapeutic intervention (e.g. paladin-specific phosphatase inhibitors).

Neurotrypsin

Neurotrypsin is a mosaic protein of 761 aa consisting of a kringle domain, followed by three scavenger receptor cysteine-rich repeats, and a serine protease domain (24-27). The protease domain belongs to the subfamily of trypsin-like serine proteases. The exact function of the protease and its mechanism of action is unknown. There are no interacting proteins known. Expression of neurotrypsin in the adult murine nervous system is confined to distinct subsets of neurons. The most prominent expression was found in the cerebral cortex, the hippocampus, and the amygdala, ie structures engaged in the processing and storage of learned behaviors and memories (24). Together with the

recently obtained evidence that extracellular serine proteases play a role in neural plasticity, this expression pattern suggests that the extracellular proteolytic action of neurotrypsin subserves structural reorganizations associated with learning and memory operations (24). The developmental expression pattern in the mouse embryo suggests roles of neurotrypsin in morphogenesis of nonneuronal tissues, as well as in neural development, in particular in axonal target invasion, synaptogenesis, and Schwann cell differentiation (28). A 4-base pair deletion in the neurotrypsin gene is associated with autosomal recessive nonsyndromic mental retardation (MR). Immuno-electron microscopy on adult human brain sections revealed that neurotrypsin is located in presynaptic nerve endings, particularly over the presynaptic membrane lining the synaptic cleft suggesting that neurotrypsin-mediated proteolysis is required for synaptic function and defects in neurotrypsin function may cause mental retardation (29).

Neurotrypsin and novel proteases associated with it may regulate Abeta secretion through BACE- and gamma-secretase dependent processing. Alternatively, Neurotrypsin may cleave APP and Abeta peptides directly. Note that APP is also localised at presynaptic nerve endings, consistent with a role of Neurotrypsin in APP processing. Neurotrypsin, its interacting proteins, and in particular its protease activity are therapeutic targets for neurodegenerative disease characterised by Abeta pathology.

Hunc-18 (Syntaxin-binding protein 1)

Hunc18a is the human ortholog of mouse Munc18a, an SM-protein that is essential for neurotransmitter release (30). It has been suggested that binding of Hunc18a to syntaxins 1a, 1b, 2 and/or 3 is required for its fusogenic function (31). Recently, a synergistic effect of Hunc18a and X11 proteins on amyloid precursor protein metabolism has been demonstrated. The molecular mechanism underlying this phenomenon is, however, not understood. However, it appears to be independent of a direct interaction of Munc18a with X11 (32).

Novel proteins associated with Hunc18a and X11 complexes are potential targets for therapeutic intervention.

Telencephalin

Telencephalin is a member of the intercellular adhesion molecule (ICAM) family, type I transmembrane glycoproteins, that contain 2-9 immunoglobulin-like C2-type domains, and bind to the leukocyte adhesion LFA-1 protein (33,34). This protein is expressed on the surface of telencephalic neurons and displays two types of adhesion activity, homophilic binding between neurons and heterophilic binding between neurons and leukocytes. It may be a critical component in neuron-microglial cell interactions in the course of normal development or as part of neurodegenerative diseases (35).

The C terminus of PS1 and PS2 binds to the telencephalin (TLN) in the brain (35). PS1 deficiency results in the abnormal accumulation of TLN in a yet unidentified intracellular compartment. The first transmembrane domain and carboxyl terminus of PS1 form a binding pocket with the transmembrane domain of TLN suggesting that a telencephalin-containing protein complex be involved in the pathogenesis of Alzheimer's disease (35).

Novel proteins associated with telencephalin and gamma-secretase complexes are potential targets for therapeutic intervention..

PC7

PC7 is a furin-like prohormone convertase that contains a 42-residue signal peptide at the N terminus, 6 potential N-linked glycosylation sites, and a 22-amino acid transmembrane region (36). It shares more than 50% amino acid identity over the catalytic region with other members of the prohormone convertase family and is structurally more closely related to PACE and PACE4 than to PC1 or PC2.

Because activation of BACE is believed to be performed by furin, but not by PC7, and activation of ADAM10 can be induced by both PC7 and furin, the competition between BACE and ADAM10 with regard to APP cleavage might be shifted to the nonamyloidogenic pathway by an inhibition of furin and/or a simultaneous stimulation of PC7. Considering the resemblance between PC7 and furin, this might be difficult to achieve. However, pathways that lead to enhanced gene expression of PC7 may be beneficial in the cause of AD (37,38).

Hence, novel proteins associated with PC7 protein complexes, in particular PC7 substrates, are potential targets for therapeutic intervention.

TFCP2

Lambert et al. (2000) described an association between a noncoding polymorphism (G-A) in the 3' untranslated region of the transcription factor TFCP2 and sporadic Alzheimer disease, suggesting a protective effect (39). The A allele demonstrated reduced binding to nuclear protein(s) from a neuroblastoma cell line, and absence of the A allele was associated with lower gene expression in lymphocytes from AD cases compared with controls. Polymorphisms in TFCP2 may hence be important for the pathogenesis of AD, particularly since the TFCP2 gene product was shown to interact with GSK3B, Fe65 , and other factors involved in the inflammatory response (39).

Novel proteins associated with the nuclear complexes of TFCP2 may play a role in the etiology of AD, e.g. in APP intracellular domain (AICD) dependent gene expression, and hence are potential targets for therapeutic intervention.

JIP1 (MAPK8IP1)

The JIP proteins (40) function by scaffolding components of a MAP kinase module (including MLK, MKK7, and JNK) and facilitate signal transmission by the protein kinase cascade (41).

Waeber et al. evaluated the role of JIP1 in beta-cells and proposed JIP-1 as a candidate gene for human diabetes. In one family a JIP1 missense mutation S59N segregated with diabetes and thus JIP1 represents a candidate susceptibility gene for type 2 diabetes (42).

Two groups presented evidence for an interaction of JIP1b with the cytoplasmic tail of APP (43-45). Another group reported a mutual relationship of the expression levels of JIP1 and alpha synuclein in cultured neurons (46). Over-expression of JIP1 has been reported to stabilize immature APP and to suppress the production of an intracellular carboxyl-terminal fragment of APP (APP intracellular domain (AICD)), and the secretion of peptides A-beta 1-40 and A-beta 1-42, the predominant constituents of amyloid plaques in Alzheimer's disease. The mechanism of JIP1's amyloidogenic function is unknown. JIP1 and related proteins JIP2 and JIP3 bind to the C-terminus of kinesin light chain suggesting that a JIP1-containing protein complex might be involved in APP trafficking (47,48).

The protein complex around JIP1 is of high potential therapeutic interest for AD and related neurodegenerative diseases because membrane-associated, cytoplasmic and nuclear complexes of the APP intracellular domain (AICD) with adaptor proteins regulate APP stability and turnover, nuclear translocation, and its transcriptional function, which are all potential targets for therapeutic intervention.

FKRP

Brockington et al. identified the fukutin-related protein gene (FKRP) by database screening using the mouse fukutin sequence and cloned fukutin-related protein (FKRP) by a combination of EST assembly, RT-PCR, and RACE (49). The cDNA encodes a 495-amino acid protein with a molecular organization similar to several Golgi-resident glycosyltransferases. Northern blot analysis detected a 4.0-kb FKRP transcript expressed predominantly in skeletal muscle, placenta, and heart and relatively weakly in other tissues.

FKRP mutations are found in families with severe and early-onset phenotypes of congenital muscular dystrophies (CMD). Structural brain defects, with or without mental retardation, are additional features of CMD. A variable reduction of alpha-dystroglycan expression was observed in the skeletal muscle biopsy of all individuals studied. In addition, several cases showed a deficiency of laminin 2 (49,50).

FKRP and fukutin are Golgi-resident proteins and FKRP is required for the post-translational modification of dystroglycan (51).

FKRP is a novel interactor of PS1. Since exit of presenilins and the active gamma-secretase complex from the ER is critical for gamma-secretase function (52), FKRP and associated proteins may play a role in regulating gamma-secretase activity and/or trafficking, allowing access to APP. Interfering with FTRP and associated proteins may be a therapeutic strategy for the treatment of AD.

VTRP

VTRP is a putative transport-related protein that was originally cloned from cultured astrocytes. It is an immediate-early gene expression of which is induced 15 min after reoxygenation(following an episode of hypoxia (53). There are no interacting proteins known.

SLY1, a member of the evolutionarily conserved Sec1/Munc-18 family of proteins, is an essential gene for vesicular transport between the ER and the cis Golgi in *S. cerevisiae*. Analogously, interaction of rat Sly1 (which is 95% identical with human VTRP) with syntaxins 5 and 18 serves an important function in regulating intracellular traffic in vertebrates (54).

Since exit of presenilins and the active gamma-secretase complex from the ER is critical for gamma-secretase function (52), VTRP and associated proteins might play a role in regulating gamma-secretase activity. Interfering with VTRP regulated trafficking events may be a therapeutic strategy for the treatment of AD.

3. SUMMARY OF THE INVENTION

An object of the present invention was to identify protein complexes of the beta-amyloid precursor protein (APP) processing pathway, component proteins of the said complexes, fragments and derivatives of the component proteins, and antibodies specific to the complexes. The present invention also relates to methods for use of the protein complexes of the APP processing pathway and their interacting proteins in, inter alia, screening, diagnosis, and therapy, as well as to methods of preparing the complexes.

By applying the process according to the invention said complexes were identified. The components are listed in table 1.

Said object is further achieved by the characterization of component proteins. These proteins are listed in table 2.

Thus, the invention relates to the following embodiments:

1. A protein complex selected from complex (I) and comprising
 - (a) at least one first protein, which first protein is selected from the group of proteins in table 1, fourth column of a given complex, or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of said protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions; and
 - (b) at least one second protein, which second protein is selected from the group of proteins in table 1, fifth column of said given complex, or a functionally active

derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of said second protein, said variant being encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions; and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4) 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

2. A protein complex comprising a first protein selected from the proteins listed in table 1, fourth column of a given complex or a homologue or variant thereof, or a functionally active fragment or functionally active derivative of said first protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said first protein under low stringency conditions, and at least one second protein selected from the group of proteins in table 1, fifth column of a given complex, or a variant or homologue thereof, or a functionally active fragment or a functionally active derivative of said second protein, the variant of said second protein being encoded by a nucleic acid that hybridizes to the nucleic acid of said second protein under low-stringency conditions, and wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4) 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.
3. A protein complex comprising all proteins selected from the proteins in table 1, third column of a given complex or at least one protein being a homologue thereof, or a variant thereof or functionally active fragment or functionally active derivative of said protein, said variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said protein under low stringency conditions;

wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

4. A protein complex that comprises all proteins as listed in table 1, third column for a given complex or at least one protein being a homologue or a variant thereof, or a functionally active fragment or a functionally active derivative thereof, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of any of said proteins under low stringency conditions, except at least one protein of the proteins listed in table 5, third column, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C, with the proviso that the complex comprises at least one protein selected from table 1, fifth column of a given complex.
5. The complex of any of No. 1 - 4 comprising at least one functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein.
6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.

7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.
8. The complex of any of No. 1 - 7 that is involved in at least one biochemical activity as stated in table 3.
9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps:
expressing a protein of the complex, preferably a tagged protein, in a target cell, or a tissue or an organ, isolating the protein complex which is attached to the protein, preferably the tagged protein, and optionally disassociating the protein complex and isolating the individual complex members.
10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.
11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.
12. Component of a protein complex obtainable by a process according to any of No. 9 - 11.
13. Protein selected from the group of proteins in table 1, sixth column of a given complex or a homologue or a variant of thereof, or a functionally active fragment or a functionally active derivative of said protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

14. Nucleic acid encoding a protein according to No. 13.
15. Construct, preferably a vector construct, comprising
 - (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or
 - (b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative thereof, or a homologue or a variant thereof, at least one of said proteins being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, being selected from the second group of proteins according to No. 1 (b) or
 - (c) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative thereof, or a homologue or a variant thereof, said proteins being selected from the proteins of complex (II) according to No. 1.
16. Host cell, containing a vector comprising at least one nucleic acid of No. 14 and /or a construct of No. 15 or containing several vectors each comprising at least one nucleic acid encoding at least one protein selected from the first group of proteins according to No. 1 (a) and at least one nucleic acid encoding at least one protein selected from the second group of proteins according to No. 1 (b).
17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody containing the binding domain thereof which binds to any of the proteins of the group of proteins according to No. 13.
18. A kit comprising in one or more containers:
 - (a) the complex of any of No. 1 – 8 and/or the proteins of No. 13 and/or
 - (b) an antibody according to No. 17 and/or
 - (c) a nucleic acid encoding a protein of the complex of any of No. 1 – 8 and/or a protein of No. 13 and/or

- (d) cells expressing the complex of any of No. 1 – 8 and/or a protein of No. 13 and, optionally,
 - (e) further components such as reagents, buffers and working instructions.
19. The kit according to No. 18 for processing a substrate of a complex of any one of No. 1 - 8.
20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as those as stated in column 2, table 4 of a given complex.
21. Array, preferably a microarray, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 13 and/or at least one antibody according to No. 17 is attached to a solid carrier.
22. A process for modifying a substrate of a complex of any one of No. 1 - 8 comprising the step of bringing into contact a complex of any of No. 1 - 8 with said substrate, such that said substrate is modified.
23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or a protein according to No. 13.
24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders, preferentially for diseases or disorders such as those as stated in column 2, table 4 of a given complex.
25. A method for screening for a molecule that binds to a complex of any one of No. 1 - 8 and/or a protein of No. 13, comprising the following steps:
- (a) exposing said complex or protein, or a cell or organism containing said complex or said protein, to one or more candidate molecules; and
 - (b) determining whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of a complex of any one of No. 1 - 8 comprising the steps of:
- (a) exposing said complex, or a cell or organism containing said complex to one or more candidate molecules; and
 - (b) determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene regulated by the complex and/or the abundance and/or activity of a protein or protein complex dependent upon the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene regulated by the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity, or composition of said complex.
27. The method of No. 26, wherein the amount of said complex is determined.
28. The method of No. 26, wherein the activity of said complex is determined.
29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.
30. The method of No. 26, wherein the amount of the individual protein components of said complex is determined.

31. The method of No. 30, wherein said determining step comprises determining whether any of the proteins listed in table 1, third column of said complex, or a functionally active fragment or a functionally active derivative thereof, or a variant or a homologue thereof, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said protein under low-stringency conditions, is present in the complex.
32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder, preferentially of a disease or disorder selected from the diseases or disorders such as those as stated in column 2, table 4 of a given complex.
33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder, preferentially of a disease or disorder such as those as stated in column 2, table 4 of a given complex.
34. A method for the production of a pharmaceutical composition comprising carrying out the method of No. 26 - 31 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.
35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, component disposition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene regulated by the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in a corresponding sample from a subject not having the disease or disorder or predisposition indicated the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.
37. The method of No. 35, wherein the activity of said complex is determined.
38. The method of No. 37, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.
39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.
40. The method of No. 39, wherein said determining step comprises determining whether any of the proteins according to No. 13 is present in the complex.
41. The complex of any one of No. 1 - 8, or a protein of No. 13 or an antibody or fragment thereof of No. 17, for use in a method of diagnosing a disease or disorder, preferentially of a disease or disorder such as neurodegenerative disease such as those as stated in column 2, table 4 of a given complex.
42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity of, component composition of or intracellular localization of, the complex of any one of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, activity of, or protein composition of, said complex.
43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.
45. Complex of No. 1 - 8 and/or a protein as listed in table 1, fifth column of said complex as a target for an active agent of a pharmaceutical, preferably a drug target, in the treatment or prevention of a disease or disorder, preferentially of a disease or disorder such as a neurodegenerative disease such as those as stated in column 2, table 4 of a given complex.

3.1 DEFINITIONS

The term "activity" as used herein, refers to the function of a molecule in its broadest sense. It generally includes, but is not limited to, biological, biochemical, physical or chemical functions of the molecule. It includes for example the enzymatic activity, the ability to interact with other molecules and ability to activate, facilitate, stabilize, inhibit, suppress or destabilize the function of other molecules, stability, ability to localize to certain subcellular locations. Where applicable, said term also relates to the function of a protein complex in its broadest sense.

The term "agonist" as used herein, means a molecule which modulates the formation of a protein complex or which, when bound to a complex or protein of the invention or a molecule in the protein complex, increases the amount of, or prolongs the duration of, the activity of the complex. The stimulation may be direct or indirect, including effects on the expression of a gene encoding a member of the protein complex, or by a competitive or non-competitive mechanism. Agonists may include proteins, nucleic acids, carbohydrates or any other organic or anorganic molecule or metals. Agonists also include a functional peptide or peptide fragment derived from a protein member of the complexes of the invention or a protein member itself of the complexes of the invention. Preferred activators are those which, when added to the complex and/or the protein of the invention under physiological conditions and/or in vitro assays, including diagnostic or prognostic assays, result in a change of the level of any of the activities of the protein complex and/or the proteins of the invention as exemplary illustrated above by at least 10%, at least 25%, at least 50%, at least 100%, at least, 200%, at least 500% or at least 1000% at a concentration of the activator $1\mu\text{g ml}^{-1}$, $10\mu\text{g ml}^{-1}$, $100\mu\text{g ml}^{-1}$, $500\mu\text{g ml}^{-1}$, 1mg ml^{-1} , 10mg ml^{-1} or 100mg ml^{-1} . Any combination of the

above mentioned degrees of percentages and concentration may be used to define an agonist of the invention, with greater effect at lower concentrations being preferred.

The term "amount" as used herein and as applicable to the embodiment described relates to the amount of the particular protein or protein complex described, including the value of null, i.e. where no protein or protein complex described in that particular embodiment is present under the or any of the conditions which might be specified in that particular embodiment.

The term "animal" as used herein includes, but is not limited to mammals, preferably mammals such as cows, pigs, horses, mice, rats, cats, dogs, sheep, goats and most preferably humans. Other animals used in agriculture, such as chickens, ducks etc. are also included in the definition as used herein.

The term "animal" as used herein does not include humans if being used in the context of genetic alterations to the germline.

The term "antagonist" as used herein, means a molecule which modulates the formation of a protein complex or which, when bound to a complex or protein of the invention or a molecule in the protein complex, decreases the amount of, or the duration or level of activity of the complex. The effect may be direct or indirect, including effects on the expression of a gene encoding a member of the protein complex, or by a competitive or non-competitive mechanism. Antagonists may include proteins, including antibodies, nucleic acids, carbohydrates or any other organic or anorganic molecule or metals. Antagonists also include a functional peptide or peptide fragment derived from a protein member of the complexes of the invention or a protein member itself of the complexes of the invention. Preferred antagonists are those which, when added to the complex and/or the protein of the invention under physiological conditions and/or in vitro assays, including diagnostic or prognostic assays, result in a change of the level of any of the activities of the protein complex and/or the proteins of the invention as exemplary illustrated above by at least 10%, at least 20%, at least 30%, at least 40% at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, at least 95% or at least 99% at a concentration of the inhibitor of $1\mu\text{g ml}^{-1}$, $10\mu\text{g ml}^{-1}$, $100\mu\text{g ml}^{-1}$, $500\mu\text{g ml}^{-1}$, 1mg ml^{-1} , 10mg ml^{-1} or 100mg ml^{-1} .

Any combination of the above mentioned degrees of percentages and concentration may be used to define antagonist of the invention, with greater effect at lower concentrations being preferred.

The term "antibodies" as used herein, include include, but are not limited to, polyclonal, monoclonal, chimeric, single chain, Fab fragments, and an Fab expression library.

The term "binding" as used herein means a stable or transient association between two molecules, including electrostatic, hydrophobic, ionic and/or hydrogen-bond interaction under physiological conditions and/or conditions being used in diagnostic or prognostic method or process or procedure.

The term "carrier" as used herein refers to a diluent, adjuvant, excipient, or vehicle with which the therapeutic is administered. Such pharmaceutical carriers can be sterile liquids, such as water and oils, including those of petroleum, animal, vegetable or synthetic origin, including but not limited to peanut oil, soybean oil, mineral oil, sesame oil and the like. Water is a preferred carrier when the pharmaceutical composition is administered orally. Saline and aqueous dextrose are preferred carriers when the pharmaceutical composition is administered intravenously. Saline solutions and aqueous dextrose and glycerol solutions are preferably employed as liquid carriers for injectable solutions. Suitable pharmaceutical excipients include starch, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, sodium stearate, glycerol monostearate, talc, sodium chloride, dried skim milk, glycerol, propylene, glycol, water, ethanol and the like. The composition, if desired, can also contain minor amounts of wetting or emulsifying agents, or pH buffering agents. These compositions can take the form of solutions, suspensions, emulsions, tablets, pills, capsules, powders, sustained-release formulations and the like. The composition can be formulated as a suppository, with traditional binders and carriers such as triglycerides. Oral formulation can include standard carriers such as pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, sodium saccharine, cellulose, magnesium carbonate, etc. Examples of suitable pharmaceutical carriers are described in "Remington's Pharmaceutical Sciences" by E.W. Martin. Such compositions will contain a therapeutically effective amount of the therapeutic, preferably in purified form, together with a suitable amount of carrier so as to provide the form for proper administration to the patient. The formulation should suit the mode of administration.

If not stated otherwise, the terms "complex" and "protein complex" are used interchangeably herein and refer to a complex of proteins that is able to perform one or more functions of the wild type protein complex. The protein complex may or may not include and/or be associated with other molecules such as nucleic acid, such as RNA or

DNA, or lipids or further cofactors or moieties selected from a metal ions, hormones, second messengers, phosphate, sugars.

A "complex" of the invention may also be part of or a unit of a larger physiological protein assembly.

The term "component of the APP processing pathway" as used herein refers to a protein and/or protein complex which is involved in mediating APP processing in a cell. Components of the APP processing pathway include the following protein complexes as provided herein and components thereof:

APP-C59-complex, Bace1-complex, Bace2-complex, BRI-complex, mDab1-complex, Fe65L2-complex, Plit-complex, Paladin-complex, Neurotrypsin-complex, Hunc18a-complex, Telencephalin-complex, PC7-complex, TFCP2-complex, Jip1-complex, Lamezin-complex, VTRP-complex, p75-NTR-complex

If not stated otherwise, the term "compound" as used herein are include but are not limited to peptides, nucleic acids, carbohydrates, natural product extract libraries organic molecules, preferentially small organic molecules, anorganic molecules, including but not limited to chemicals, metals and organometallic molecules.

The terms "derivatives" or "analogs of component proteins" or "variants" as used herein include, but are not limited, to molecules comprising regions that are substantially homologous to the component proteins, in various embodiments, by at least 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95% or 99% identity over an amino acid sequence of identical size or when compared to an aligned sequence in which the alignment is done by a computer homology program known in the art, or whose encoding nucleic acid is capable of hybridizing to a sequence encoding the component protein under stringent, moderately stringent, or nonstringent conditions. It means a protein which is the outcome of a modification of the naturally occurring protein, by amino acid substitutions, deletions and additions, respectively, which derivatives still exhibit the biological function of the naturally occurring protein although not necessarily to the same degree. The biological function of such proteins can e.g. be examined by suitable available in vitro assays as provided in the invention.

The term "functionally active" as used herein refers to a polypeptide, namely a fragment or derivative, having structural, regulatory, or biochemical functions of the protein according to the embodiment of which this polypeptide, namely fragment or derivative is related to.

The term "fragment" as used herein refers to a polypeptide of at least 10, 20, 30, 40 or 50 amino acids of the component protein according to the embodiment. In specific embodiments, such fragments are not larger than 35, 100 or 200 amino acids.

The term "gene" as used herein refers to a nucleic acid comprising an open reading frame encoding a polypeptide of, if not stated otherwise, the present invention, including both exon and optionally intron sequences.

The terms "homologue" or "homologous gene products" as used herein mean a protein in another species, preferably mammals, which performs the same biological function as the a protein component of the complex further described herein. Such homologues are also termed "orthologous gene products". The algorithm for the detection of orthologue gene pairs from humans and mammals or other species uses the whole genome of these organisms. First, pairwise best hits are retrieved, using a full Smith-Waterman alignment of predicted proteins. To further improve reliability, these pairs are clustered with pairwise best hits involving *Drosophila melanogaster* and *C. elegans* proteins. Such analysis is given, e.g., in *Nature*, 2001, 409:860-921. The homologues of the proteins according to the invention can either be isolated based on the sequence homology of the genes encoding the proteins provided herein to the genes of other species by cloning the respective gene applying conventional technology and expressing the protein from such gene, or by isolating proteins of the other species by isolating the analogous complex according to the methods provided herein or to other suitable methods commonly known in the art.

The term "host cells" or, were applicable, "cells" or "hosts" as used herein is intended to be understood in a broadest sense and include, but are not limited to mammalian cell systems infected with virus (e.g., vaccinia virus, adenovirus, etc.); insect cell systems infected with virus (e.g., baculovirus); microorganisms such as yeast containing yeast vectors; or bacteria transformed with bacteriophage, DNA, plasmid DNA, or cosmid DNA. The expression elements of vectors vary in their strengths and specificities. Depending on the host-vector system utilized, any one of a number of suitable transcription and translation elements may be used. It is understood that this term not only refers to the particular subject cell but to the progeny or potential progeny of such a cell. Because certain modifications may occur in succeeding generations due to either mutation or environmental influences, such progeny may not, in fact, be identical to the parent cell, but are still included within the scope of the term as used herein.

The term "modification" as used herein refers to all modifications of a protein or protein complex of the invention including cleavage and addition or removal of a group.

The term "nucleic acid" as used herein refers to polynucleotides such as deoxyribonucleic acid (DNA), and, where appropriate, ribonucleic acid (RNA). They may also be polynucleotides which include within them synthetic or modified nucleotides. A number of different types of modification to polynucleotides are known in the art. These include methylphosphonate and phosphorothioate backbones, addition of acridine or polylysine chains at the 3' and/or 5' ends of the molecule. For the purposes of the present invention, it is to be understood that the polynucleotides described herein may be modified by any method available in the art. Such modifications may be carried out in order to enhance the *in vivo* activity or lifespan of polynucleotides of the invention. Polynucleotides according to the invention may be produced recombinantly, synthetically, or by any means available to those of skill in the art. They may also be cloned by standard techniques. The polynucleotides are typically provided in isolated and/or purified form. As applicable to the embodiment being described, they include both single stranded and double-stranded polynucleotides.

The term "percent identity", as used herein, means the number of identical residues as defined by an optimal alignment using the Smith-Waterman algorithm divided by the length of the overlap multiplied by 100. The alignment is performed by the search program (Pearson, 1991, Genomics 11:635-650) with the constraint to align the maximum of both sequences.

The terms "polypeptides" and "proteins" are, where applicable, used interchangeably herein. They may be chemically modified, e.g. post-translationally modified. For example, they may be glycosylated or comprise modified amino acid residues. They may also be modified by the addition of a signal sequence to promote their secretion from a cell where the polypeptide does not naturally contain such a sequence. They may be tagged with a tag. They may be tagged with different labels which may assist in identification of the proteins in a protein complex. Polypeptides/proteins for use in the invention may be in a substantially isolated form. It will be understood that the polypeptide/protein may be mixed with carriers or diluents which will not interfere with the intended purpose of the polypeptide and still be regarded as substantially isolated. A polypeptide/protein for use in the invention may also be in a substantially purified form, in which case it will generally comprise the polypeptide in a

preparation in which more than 50%, e.g. more than 80%, 90%, 95% or 99%, by weight of the polypeptide in the preparation is a polypeptide of the invention.

"Target for therapeutic drug" means that the respective protein (target) can bind the active ingredient of a pharmaceutical composition and thereby changes its biological activity in response to the drug binding.

The term "tag" as used herein is meant to be understood in its broadest sense and to include, but is not limited to any suitable enzymatic, fluorescent, or radioactive labels and suitable epitopes, including but not limited to HA-tag, Myc-tag, T7, His-tag, FLAG-tag, Calmodulin binding proteins, glutathione-S-transferase, strep-tag, KT3-epitope, EEF-epitopes, green-fluorescent protein and variants thereof.

The term "therapeutics" as used herein, includes, but is not limited to, a protein complex of the present invention, the individual component proteins, and analogs and derivatives (including fragments); antibodies thereto; nucleic acids encoding the component protein, and analogs or derivatives thereof; component protein antisense nucleic acids, and agents that modulate complex formation and/or activity (i.e., agonists and antagonists).

The term "vector" as used herein means a nucleic acid molecule capable of transporting another nucleic acid sequence to which it has been linked. Preferred vectors are those capable of autonomous replication and/or expression of nucleic acids to which they linked. The terms "plasmid" and "vector" are used interchangeably herein when applicable to the embodiment. However, vectors other than plasmids are also included herein. The expression elements of vectors vary in their strengths and specificities. Depending on the host-vector system utilized, any one of a number of suitable transcription and translation elements may be used.

4. DETAILED DESCRIPTION OF THE INVENTION

Overview:

An object of the present invention was to identify protein complexes of the beta-amyloid precursor protein (APP) processing pathway, component proteins of the said complexes, fragments and derivatives of the component proteins, and antibodies specific to the complexes. The present invention also relates to methods for use of the protein

complexes of the APP processing pathway and their interacting proteins in, inter alia, screening, diagnosis, and therapy, as well as to methods of preparing the complexes.

By applying the process according to the invention said protein complex were identified. The components are listed in table 1.

Said object is further achieved by the characterisation of component proteins. These proteins are listed in table 2.

The invention thus relates to the following embodiments:

1. A protein complex selected from complex (I) and comprising
 - (a) at least one first protein, which first protein is selected from the group of proteins in table 1, fourth column of a given complex, or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of said protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions; and
 - (b) at least one second protein, which second protein is selected from the group of proteins in table 1, fifth column of said given complex, or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of said second protein, said variant being encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions; and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4) 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.
2. A protein complex comprising a first protein selected from the proteins listed in table 1, fourth column of a given complex or a homologue or variant thereof, or a functionally active fragment or functionally active derivative of said first protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said first

protein under low stringency conditions, and at least one second protein selected from the group of proteins in table 1, fifth column of a given complex, or a variant or homologue thereof, or a functionally active fragment or a functionally active derivative of said second protein, the variant of said second protein being encoded by a nucleic acid that hybridizes to the nucleic acid of said second protein under low-stringency conditions, and wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4) 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

3. A protein complex comprising all proteins selected from the proteins in table 1, third column of a given complex or at least one protein being a homologue thereof, or a variant thereof or functionally active fragment or functionally active derivative of said protein, said variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said protein under low stringency conditions; wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.
4. A protein complex that comprises all proteins as listed in table 1, third column for a given complex or at least one protein being a homologue or a variant thereof, or a functionally active fragment or a functionally active derivative thereof, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of any of said proteins under low stringency conditions, except at least one protein of the proteins listed in table 5, third column, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon

sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C, with the proviso that the complex comprises at least one protein selected from table 1, fifth column of a given complex.

5. The complex of any of No. 1 - 4 comprising at least one functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein.
6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.
7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.
8. The complex of any of No. 1 - 7 that is involved in at least one biochemical activity as stated in table 3.
9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps:
expressing a protein of the complex, preferably a tagged protein, in a target cell, or a tissue or an organ, isolating the protein complex which is attached to the protein, preferably the tagged protein, and optionally disassociating the protein complex and isolating the individual complex members.
10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.

11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.
12. Component of a protein complex obtainable by a process according to any of No. 9 - 11.
13. Protein selected from the group of proteins in table 1, sixth column of a given complex or a homologue or a variant of thereof, or a functionally active fragment or a functionally active derivative of said protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.
14. Nucleic acid encoding a protein according to No. 13.
15. Construct, preferably a vector construct, comprising
 - (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or
 - (b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative thereof, or a homologue or a variant thereof, at least one of said proteins being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, being selected from the second group of proteins according to No. 1 (b) or
 - (c) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative thereof, or a homologue or a variant thereof, said proteins being selected from the proteins of complex (II) according to No. 1.

16. Host cell, containing a vector comprising at least one nucleic acid of No. 14 and /or a construct of No. 15 or containing several vectors each comprising at least one nucleic acid encoding at least one protein selected from the first group of proteins according to No. 1 (a) and at least one nucleic acid encoding at least one protein selected from the second group of proteins according to No. 1 (b).
17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody containing the binding domain thereof which binds to any of the proteins of the group of proteins according to No. 13.
18. A kit comprising in one or more containers:
 - (a) the complex of any of No. 1 – 8 and/or the proteins of No. 13 and/or
 - (b) an antibody according to No. 17 and/or
 - (c) a nucleic acid encoding a protein of the complex of any of No. 1 – 8 and/or a protein of No. 13 and/or
 - (d) cells expressing the complex of any of No. 1 – 8 and/or a protein of No. 13 and, optionally,
 - (e) further components such as reagents, buffers and working instructions.
19. The kit according to No. 18 for processing a substrate of a complex of any one of No. 1 - 8.
20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as those as stated in column 2, table 4 of a given complex.
21. Array, preferably a microarray, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 13 and/or at least one antibody according to No. 17 is attached to a solid carrier.

22. A process for modifying a substrate of a complex of any one of No. 1 - 8 comprising the step of bringing into contact a complex of any of No. 1 - 8 with said substrate, such that said substrate is modified.
23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or a protein according to No. 13.
24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders, preferentially for diseases or disorders such as those as stated in column 2, table 4 of a given complex.
25. A method for screening for a molecule that binds to a complex of any one of No. 1 - 8 and/or a protein of No. 13, comprising the following steps:
 - (a) exposing said complex or protein, or a cell or organism containing said complex or said protein, to one or more candidate molecules; and
 - (b) determining whether said candidate molecule is bound to the complex or protein.
26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of a complex of any one of No. 1 - 8 comprising the steps of:
 - (a) exposing said complex, or a cell or organism containing said complex to one or more candidate molecules; and
 - (b) determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene regulated by the complex and/or the abundance and/or activity of a protein or protein complex dependent upon the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene regulated by the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules

indicates that the molecule modulates function, activity, or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.
28. The method of No. 26, wherein the activity of said complex is determined.
29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.
30. The method of No. 26, wherein the amount of the individual protein components of said complex is determined.
31. The method of No. 30, wherein said determining step comprises determining whether any of the proteins listed in table 1, third column of said complex, or a functionally active fragment or a functionally active derivative thereof, or a variant or a homologue thereof, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said protein under low-stringency conditions, is present in the complex.
32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder, preferentially of a disease or disorder selected from the diseases or disorders such as those as stated in column 2, table 4 of a given complex.
33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder, preferentially of a disease or disorder such as those as stated in column 2, table 4 of a given complex.

34. A method for the production of a pharmaceutical composition comprising carrying out the method of No. 26 - 31 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.
35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, component disposition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene regulated by the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in a corresponding sample from a subject not having the disease or disorder or predisposition indicated the presence in the subject of the disease or disorder or predisposition in the subject.
36. The method of No. 35, wherein the amount of said complex is determined.
37. The method of No. 35, wherein the activity of said complex is determined.
38. The method of No. 37, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.
39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.
40. The method of No. 39, wherein said determining step comprises determining whether any of the proteins according to No. 13 is present in the complex.

41. The complex of any one of No. 1 - 8, or a protein of No. 13 or an antibody or fragment thereof of No. 17, for use in a method of diagnosing a disease or disorder, preferentially of a disease or disorder such as neurodegenerative disease such as those as stated in column 2, table 4 of a given complex.
42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity of, component composition of or intracellular localization of, the complex of any one of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, activity of, or protein composition of, said complex.
43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.
44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.
45. Complex of No. 1 - 8 and/or a protein as listed in table 1, fifth column of said complex as a target for an active agent of a pharmaceutical, preferably a drug target, in the treatment or prevention of a disease or disorder, preferentially of a disease or disorder such as a neurodegenerative disease such as those as stated in column 2, table 4 of a given complex.

Animal models are also provided herein.

Preferably, the protein components of the complexes described herein are all mammalian proteins. The complexes can also consist only of the respective homologues from other mammals such as mouse, rat, pig, cow, dog, monkey, sheep or horse or other species such as *D. melanogaster*, *C. elegans* or chicken. In another preferred embodiment, the complexes are a mixture of proteins from two or more species.

TABLES:

Table 1: Composition of Complexes

First column ('Name of complex'): Lists the name of the protein complexes as used herein.

Second column ('Entry point'): Lists the bait proteins that have been chosen for the purification of the given complex.

Third column ('All interactors'): Lists all novel interactors which have been identified as members of the complex and all interactors which have been known to be associated with the bait so far.

Fourth column ('Known interactors'): Lists all interactors which have been known to be associated with the bait so far.

Fifth column ('Novel interactors of the complex'): Lists all novel interactors of the complex which have been identified in the experiments provided herein.

Sixth column: Separately lists the members of the newly identified complex which have not been annotated previously.

Table 2: Individual Proteins of the Complexes

First column ('Protein'): Lists in alphabetical order all proteins which have been identified as interactors of the complexes presented herein.

Second column ('SEQ ID'): Lists the SEQ ID (Sequence Identifications) of the proteins herein as used herein.

Third column ('IPI-Numbers'): Lists the IPI-Numbers of the proteins herein. The IPI-Numbers refer to the International Protein Index created by the European Bioinformatics Institute (EMBL-EBI), Hinxton, UK.

Fourth column ('Molecular Weight'): Lists the Molecular Weight of the proteins in Dalton.

Table 3: Biochemical Activities of the Complexes of the invention.

First column ('Name of complex'): Lists the name of the protein complexes as used herein.

Second column ('Biochemical Activity'): Lists biochemical activities of the complexes. Assays in order to test these activities are also provided herein (infra).

Table 4: Medical Applications of the Complexes of the invention

First column ('Name of complex'): Lists the name of the protein complexes as used herein

Second column ('Medical application'): lists disorder, diseases, disease areas etc. which are treatable and/or preventable and/or diagnosable etc. by therapeutics and methods interacting with/acting via the complex.

4.1 PROTEIN COMPLEXES/PROTEINS OF THE INVENTION

The protein complexes of the present invention and their component proteins are described in the Tables 1 - 4. The protein complexes and component proteins can be obtained by methods well known in the art for protein purification and recombinant protein expression. For example, the protein complexes of the present invention can be isolated using the TAP method described in Section 5, infra, and in WO 00/09716 and Rigaut et al., 1999, *Nature Biotechnol.* 17:1030-1032, which are each incorporated by reference in their entirety. Additionally, the protein complexes can be isolated by immunoprecipitation of the component proteins and combining the immunoprecipitated proteins. The protein complexes can also be produced by recombinantly expressing the component proteins and combining the expressed proteins.

The nucleic and amino acid sequences of the component proteins of the protein complexes of the present invention are provided herein (SEQ ID NO 1 - 249), and can be obtained by any method known in the art, e.g., by PCR amplification using synthetic primers hybridizable to the 3' and 5' ends of each sequence, and/or by cloning from a cDNA or genomic library using an oligonucleotide specific for each nucleotide sequence.

Homologues (e.g., nucleic acids encoding component proteins from other species) or other related sequences (e.g., variants, paralogs) which are members of a native cellular protein complex can be obtained by low, moderate or high stringency hybridization with all or a portion of the particular nucleic acid sequence as a probe, using methods well known in the art for nucleic acid hybridization and cloning.

Exemplary moderately stringent hybridization conditions are as follows: prehybridization of filters containing DNA is carried out for 8 hours to overnight at 65°C in buffer composed of 6X SSC, 50 mM Tris-HCl (pH 7.5), 1 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.02% BSA, and 500 µg/ml denatured salmon sperm DNA. Filters are hybridized for 48 hours at 65°C in prehybridization mixture containing 100 µg/ml denatured salmon sperm DNA and 5-20 X 10⁶ cpm of ³²P-labeled probe. Washing of filters is done at 37°C

for 1 hour in a solution containing 2X SSC, 0.01% PVP, 0.01% Ficoll, and 0.01% BSA. This is followed by a wash in 0.1X SSC at 50 °C for 45 min before autoradiography. Alternatively, exemplary conditions of high stringency are as follows: e.g., hybridization to filter-bound DNA in 0.5 M NaHPO₄, 7% sodium dodecyl sulfate (SDS), 1 mM EDTA at 65°C, and washing in 0.1xSSC/0.1% SDS at 68°C (Ausubel et al., eds., 1989, Current Protocols in Molecular Biology, Vol. I, Green Publishing Associates, Inc., and John Wiley & sons, Inc., New York, at p. 2.10.3). Other conditions of high stringency which may be used are well known in the art. Exemplary low stringency hybridization conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 µg/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

For recombinant expression of one or more of the proteins, the nucleic acid containing all or a portion of the nucleotide sequence encoding the protein can be inserted into an appropriate expression vector, i.e., a vector that contains the necessary elements for the transcription and translation of the inserted protein coding sequence. The necessary transcriptional and translational signals can also be supplied by the native promoter of the component protein gene, and/or flanking regions.

A variety of host-vector systems may be utilized to express the protein coding sequence. These include but are not limited to mammalian cell systems infected with virus (e.g., vaccinia virus, adenovirus, etc.); insect cell systems infected with virus (e.g., baculovirus); microorganisms such as yeast containing yeast vectors; or bacteria transformed with bacteriophage, DNA, plasmid DNA, or cosmid DNA. The expression elements of vectors vary in their strengths and specificities. Depending on the host-vector system utilized, any one of a number of suitable transcription and translation elements may be used.

In a preferred embodiment, a complex of the present invention is obtained by expressing the entire coding sequences of the component proteins in the same cell, either under the control of the same promoter or separate promoters. In yet another embodiment, a derivative, fragment or homologue of a component protein is recombinantly expressed. Preferably the derivative, fragment or homologue of the protein forms a complex with the other components of the complex, and more preferably

forms a complex that binds to an anti-complex antibody. Such an antibody is further described infra.

Any method available in the art can be used for the insertion of DNA fragments into a vector to construct expression vectors containing a chimeric gene consisting of appropriate transcriptional/translational control signals and protein coding sequences. These methods may include in vitro recombinant DNA and synthetic techniques and in vivo recombinant techniques (genetic recombination). Expression of nucleic acid sequences encoding a component protein, or a derivative, fragment or homologue thereof, may be regulated by a second nucleic acid sequence so that the gene or fragment thereof is expressed in a host transformed with the recombinant DNA molecule(s). For example, expression of the proteins may be controlled by any promoter/enhancer known in the art. In a specific embodiment, the promoter is not native to the gene for the component protein. Promoters that may be used can be selected from among the many known in the art, and are chosen so as to be operative in the selected host cell.

In a specific embodiment, a vector is used that comprises a promoter operably linked to nucleic acid sequences encoding a component protein, or a fragment, derivative or homologue thereof, one or more origins of replication, and optionally, one or more selectable markers (e.g., an antibiotic resistance gene).

In another specific embodiment, an expression vector containing the coding sequence, or a portion thereof, of a component protein, either together or separately, is made by subcloning the gene sequences into the EcoRI restriction site of each of the three pGEX vectors (glutathione S-transferase expression vectors; Smith and Johnson, 1988, Gene 7:31-40). This allows for the expression of products in the correct reading frame.

Expression vectors containing the sequences of interest can be identified by three general approaches: (a) nucleic acid hybridization, (b) presence or absence of "marker" gene function, and (c) expression of the inserted sequences. In the first approach, coding sequences can be detected by nucleic acid hybridization to probes comprising sequences homologous and complementary to the inserted sequences. In the second approach, the recombinant vector/host system can be identified and selected based upon the presence or absence of certain "marker" functions (e.g., resistance to antibiotics, occlusion body formation in baculovirus, etc.) caused by insertion of the sequences of interest in the vector. For example, if a component protein gene, or portion

thereof, is inserted within the marker gene sequence of the vector, recombinants containing the encoded protein or portion will be identified by the absence of the marker gene function (e.g., loss of β -galactosidase activity). In the third approach, recombinant expression vectors can be identified by assaying for the component protein expressed by the recombinant vector. Such assays can be based, for example, on the physical or functional properties of the interacting species in in vitro assay systems, e.g., formation of a complex comprising the protein or binding to an anti-complex antibody.

Once recombinant component protein molecules are identified and the complexes or individual proteins isolated, several methods known in the art can be used to propagate them. Using a suitable host system and growth conditions, recombinant expression vectors can be propagated and amplified in quantity. As previously described, the expression vectors or derivatives which can be used include, but are not limited to, human or animal viruses such as vaccinia virus or adenovirus; insect viruses such as baculovirus, yeast vectors; bacteriophage vectors such as lambda phage; and plasmid and cosmid vectors.

In addition, a host cell strain may be chosen that modulates the expression of the inserted sequences, or modifies or processes the expressed proteins in the specific fashion desired. Expression from certain promoters can be elevated in the presence of certain inducers; thus expression of the genetically-engineered component proteins may be controlled. Furthermore, different host cells have characteristic and specific mechanisms for the translational and post-translational processing and modification (e.g., glycosylation, phosphorylation, etc.) of proteins. Appropriate cell lines or host systems can be chosen to ensure that the desired modification and processing of the foreign protein is achieved. For example, expression in a bacterial system can be used to produce an unglycosylated core protein, while expression in mammalian cells ensures "native" glycosylation of a heterologous protein. Furthermore, different vector/host expression systems may effect processing reactions to different extents.

In other specific embodiments, a component protein or a fragment, homologue or derivative thereof, may be expressed as fusion or chimeric protein product comprising the protein, fragment, homologue, or derivative joined via a peptide bond to a heterologous protein sequence of a different protein. Such chimeric products can be made by ligating the appropriate nucleic acid sequences encoding the desired amino acids to each other by methods known in the art, in the proper coding frame, and expressing the chimeric products in a suitable host by methods commonly known in the

art. Alternatively, such a chimeric product can be made by protein synthetic techniques, e.g., by use of a peptide synthesizer. Chimeric genes comprising a portion of a component protein fused to any heterologous protein-encoding sequences may be constructed.

In particular, protein component derivatives can be made by altering their sequences by substitutions, additions or deletions that provide for functionally equivalent molecules. Due to the degeneracy of nucleotide coding sequences, other DNA sequences that encode substantially the same amino acid sequence as a component gene or cDNA can be used in the practice of the present invention. These include but are not limited to nucleotide sequences comprising all or portions of the component protein gene that are altered by the substitution of different codons that encode a functionally equivalent amino acid residue within the sequence, thus producing a silent change. Likewise, the derivatives of the invention include, but are not limited to, those containing, as a primary amino acid sequence, all or part of the amino acid sequence of a component protein, including altered sequences in which functionally equivalent amino acid residues are substituted for residues within the sequence resulting in a silent change. For example, one or more amino acid residues within the sequence can be substituted by another amino acid of a similar polarity that acts as a functional equivalent, resulting in a silent alteration. Substitutes for an amino acid within the sequence may be selected from other members of the class to which the amino acid belongs. For example, the nonpolar (hydrophobic) amino acids include alanine, leucine, isoleucine, valine, proline, phenylalanine, tryptophan and methionine. The polar neutral amino acids include glycine, serine, threonine, cysteine, tyrosine, asparagine, and glutamine. The positively charged (basic) amino acids include arginine, lysine and histidine. The negatively charged (acidic) amino acids include aspartic acid and glutamic acid.

In a specific embodiment, up to 1%, 2%, 5%, 10%, 15% or 20% of the total number of amino acids in the wild type protein are substituted or deleted; or 1, 2, 3, 4, 5, or 6 or up to 10 or up to 20 amino acids are inserted, substituted or deleted relative to the wild type protein.

In a specific embodiment of the invention, the nucleic acids encoding a protein component and protein components consisting of or comprising a fragment of or consisting of at least 6 (continuous) amino acids of the protein are provided. In other embodiments, the fragment consists of at least 10, 20, 30, 40, or 50 amino acids of the

component protein. In specific embodiments, such fragments are not larger than 35, 100 or 200 amino acids. Derivatives or analogs of component proteins include, but are not limited, to molecules comprising regions that are substantially homologous to the component proteins, in various embodiments, by at least 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95% or 99% identity over an amino acid sequence of identical size or when compared to an aligned sequence in which the alignment is done by a computer homology program known in the art, or whose encoding nucleic acid is capable of hybridizing to a sequence encoding the component protein under stringent, moderately stringent, or nonstringent conditions.

In a specific embodiment, proteins are provided herein, which share an identical region of 20, 30, 40, 50 or 60 contiguous amino acids of the proteins listed in table 2.

The protein component derivatives and analogs of the invention can be produced by various methods known in the art. The manipulations which result in their production can occur at the gene or protein level. For example, the cloned gene sequences can be modified by any of numerous strategies known in the art (Sambrook et al., 1989, Molecular Cloning, A Laboratory Manual, 2d Ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York). The sequences can be cleaved at appropriate sites with restriction endonuclease(s), followed by further enzymatic modification if desired, isolated, and ligated in vitro. In the production of the gene encoding a derivative, homologue or analog of a component protein, care should be taken to ensure that the modified gene retains the original translational reading frame, uninterrupted by translational stop signals, in the gene region where the desired activity is encoded.

Additionally, the encoding nucleic acid sequence can be mutated in vitro or in vivo, to create and/or destroy translation, initiation, and/or termination sequences, or to create variations in coding regions and/or form new restriction endonuclease sites or destroy pre-existing ones, to facilitate further in vitro modification. Any technique for mutagenesis known in the art can be used, including but not limited to, chemical mutagenesis and in vitro site-directed mutagenesis (Hutchinson et al., 1978, J. Biol. Chem. 253:6551-6558), amplification with PCR primers containing a mutation, etc.

Once a recombinant cell expressing a component protein, or fragment or derivative thereof, is identified, the individual gene product or complex can be isolated and analyzed. This is achieved by assays based on the physical and/or functional properties of the protein or complex, including, but not limited to, radioactive labeling of

the product followed by analysis by gel electrophoresis, immunoassay, cross-linking to marker-labeled product, etc.

The component proteins and complexes may be isolated and purified by standard methods known in the art (either from natural sources or recombinant host cells expressing the complexes or proteins), including but not restricted to column chromatography (e.g., ion exchange, affinity, gel exclusion, reversed-phase high pressure, fast protein liquid, etc.), differential centrifugation, differential solubility, or by any other standard technique used for the purification of proteins. Functional properties may be evaluated using any suitable assay known in the art.

Alternatively, once a component protein or its derivative, is identified, the amino acid sequence of the protein can be deduced from the nucleic acid sequence of the chimeric gene from which it was encoded. As a result, the protein or its derivative can be synthesized by standard chemical methods known in the art (e.g., Hunkapiller et al., 1984, *Nature* 310:105-111).

Manipulations of component protein sequences may be made at the protein level. Included within the scope of the invention is a complex in which the component proteins or derivatives and analogs that are differentially modified during or after translation, e.g., by glycosylation, acetylation, phosphorylation, amidation, derivatization by known protecting/blocking groups, proteolytic cleavage, linkage to an antibody molecule or other cellular ligand, etc. Any of numerous chemical modifications may be carried out by known techniques, including but not limited to specific chemical cleavage by cyanogen bromide, trypsin, chymotrypsin, papain, V8 protease, NaBH₄, acetylation, formylation, oxidation, reduction, metabolic synthesis in the presence of tunicamycin, etc.

In specific embodiments, the amino acid sequences are modified to include a fluorescent label. In another specific embodiment, the protein sequences are modified to have a heterofunctional reagent; such heterofunctional reagents can be used to crosslink the members of the complex.

In addition, complexes of analogs and derivatives of component proteins can be chemically synthesized. For example, a peptide corresponding to a portion of a component protein, which comprises the desired domain or mediates the desired activity in vitro (e.g., complex formation) can be synthesized by use of a peptide synthesizer. Furthermore, if desired, non-classical amino acids or chemical amino acid analogs can be introduced as a substitution or addition into the protein sequence.

In cases where natural products are suspected of being mutant or are isolated from new species, the amino acid sequence of a component protein isolated from the natural source, as well as those expressed in vitro, or from synthesized expression vectors in vivo or in vitro, can be determined from analysis of the DNA sequence, or alternatively, by direct sequencing of the isolated protein. Such analysis can be performed by manual sequencing or through use of an automated amino acid sequenator.

The complexes can also be analyzed by hydrophilicity analysis (Hopp and Woods, 1981, Proc. Natl. Acad. Sci. USA 78:3824-3828). A hydrophilicity profile can be used to identify the hydrophobic and hydrophilic regions of the proteins, and help predict their orientation in designing substrates for experimental manipulation, such as in binding experiments, antibody synthesis, etc. Secondary structural analysis can also be done to identify regions of the component proteins, or their derivatives, that assume specific structures (Chou and Fasman, 1974, Biochemistry 13:222-23). Manipulation, translation, secondary structure prediction, hydrophilicity and hydrophobicity profile predictions, open reading frame prediction and plotting, and determination of sequence homologies, etc., can be accomplished using computer software programs available in the art.

Other methods of structural analysis including but not limited to X-ray crystallography (Engstrom, 1974, Biochem. Exp. Biol. 11:7-13), mass spectroscopy and gas chromatography (Methods in Protein Science, J. Wiley and Sons, New York, 1997), and computer modeling (Fletterick and Zoller, eds., 1986, Computer Graphics and Molecular Modeling, In: Current Communications in Molecular Biology, Cold Spring Harbor Laboratory, Cold Spring Harbor Press, New York) can also be employed.

4.2 ANTIBODIES TO PROTEIN COMPLEXES/PROTEINS OF THE INVENTION

According to the present invention, a protein complex of the present invention comprising a first protein, or a functionally active fragment or functionally active derivative thereof, selected from the group consisting of proteins listed in fourth column of table 1; and a second protein, or a functionally active fragment or functionally active derivative thereof, selected from the group consisting of proteins listed in fifth column of table 1, or a functionally active fragment or functionally active derivative thereof, can be used as an immunogen to generate antibodies which immunospecifically bind such

immunogen. According to the present invention, also a protein complex of the present invention can be used as an immunogen to generate antibodies which immunospecifically bind to such immunogen comprising all proteins listed in fifth column of table 1.

Such antibodies include, but are not limited to, polyclonal, monoclonal, chimeric, single chain, Fab fragments, and an Fab expression library. In a specific embodiment, antibodies to a complex comprising human protein components are produced. In another embodiment, a complex formed from a fragment of said first protein and a fragment of said second protein, which fragments contain the protein domain that interacts with the other member of the complex, are used as an immunogen for antibody production. In a preferred embodiment, the antibody specific for the complex in that the antibody does not bind the individual protein components of the complex.

Polyclonal antibodies can be prepared as described above by immunizing a suitable subject with a polypeptide of the invention as an immunogen. Preferred polyclonal antibody compositions are ones that have been selected for antibodies directed against a polypeptide or polypeptides of the invention. Particularly preferred polyclonal antibody preparations are ones that contain only antibodies directed against a polypeptide or polypeptides of the invention. Particularly preferred immunogen compositions are those that contain no other human proteins such as, for example, immunogen compositions made using a non-human host cell for recombinant expression of a polypeptide of the invention. In such a manner, the only human epitope or epitopes recognized by the resulting antibody compositions raised against this immunogen will be present as part of a polypeptide or polypeptides of the invention.

The antibody titer in the immunized subject can be monitored over time by standard techniques, such as with an enzyme linked immunosorbent assay (ELISA) using immobilized polypeptide. If desired, the antibody molecules can be isolated from the mammal (e.g., from the blood) and further purified by well-known techniques, such as protein A chromatography to obtain the IgG fraction. Alternatively, antibodies specific for a protein or polypeptide of the invention can be selected for (e.g., partially purified) or purified by, e.g., affinity chromatography. For example, a recombinantly expressed and purified (or partially purified) protein of the invention is produced as described herein, and covalently or non-covalently coupled to a solid support such as, for example, a chromatography column. The column can then be used to affinity purify antibodies

specific for the proteins of the invention from a sample containing antibodies directed against a large number of different epitopes, thereby generating a substantially purified antibody composition, i.e., one that is substantially free of contaminating antibodies. By a substantially purified antibody composition is meant, in this context, that the antibody sample contains at most only 30% (by dry weight) of contaminating antibodies directed against epitopes other than those on the desired protein or polypeptide of the invention, and preferably at most 20%, yet more preferably at most 10%, and most preferably at most 5% (by dry weight) of the sample is contaminating antibodies. A purified antibody composition means that at least 99% of the antibodies in the composition are directed against the desired protein or polypeptide of the invention.

At an appropriate time after immunization, e.g., when the specific antibody titers are highest, antibody-producing cells can be obtained from the subject and used to prepare monoclonal antibodies by standard techniques, such as the hybridoma technique originally described by Kohler and Milstein, 1975, *Nature* 256:495-497, the human B cell hybridoma technique (Kozbor et al., 1983, *Immunol. Today* 4:72), the EBV-hybridoma technique (Cole et al., 1985, *Monoclonal Antibodies and Cancer Therapy*, Alan R. Liss, Inc., pp. 77-96) or trioma techniques. The technology for producing hybridomas is well known (see generally *Current Protocols in Immunology* 1994, Coligan et al. (eds.) John Wiley & Sons, Inc., New York, NY). Hybridoma cells producing a monoclonal antibody of the invention are detected by screening the hybridoma culture supernatants for antibodies that bind the polypeptide of interest, e.g., using a standard ELISA assay.

Alternative to preparing monoclonal antibody-secreting hybridomas, a monoclonal antibody directed against a polypeptide of the invention can be identified and isolated by screening a recombinant combinatorial immunoglobulin library (e.g., an antibody phage display library) with the polypeptide of interest. Kits for generating and screening phage display libraries are commercially available (e.g., the Pharmacia Recombinant Phage Antibody System, Catalog No. 27-9400-01; and the Stratagene SurfZAP Phage Display Kit, Catalog No. 240612). Additionally, examples of methods and reagents particularly amenable for use in generating and screening antibody display library can be found in, for example, U.S. Patent No. 5,223,409; PCT Publication No. WO 92/18619; PCT Publication No. WO 91/17271; PCT Publication No. WO 92/20791; PCT Publication No. WO 92/15679; PCT Publication No. WO 93/01288; PCT Publication No. WO 92/01047; PCT Publication No. WO 92/09690; PCT Publication No. WO 90/02809; Fuchs et al.,

1991, Bio/Technology 9:1370-1372; Hay et al., 1992, Hum. Antibod. Hybridomas 3:81-85; Huse et al., 1989, Science 246:1275-1281; Griffiths et al., 1993, EMBO J. 12:725-734.

Additionally, recombinant antibodies, such as chimeric and humanized monoclonal antibodies, comprising both human and non-human portions, which can be made using standard recombinant DNA techniques, are within the scope of the invention. A chimeric antibody is a molecule in which different portions are derived from different animal species, such as those having a variable region derived from a murine mAb and a human immunoglobulin constant region. (See, e.g., Cabilly et al., U.S. Patent No. 4,816,567; and Boss et al., U.S. Patent No. 4,816,397, which are incorporated herein by reference in their entirety.) Humanized antibodies are antibody molecules from non-human species having one or more complementarily determining regions (CDRs) from the non-human species and a framework region from a human immunoglobulin molecule. (See, e.g., Queen, U.S. Patent No. 5,585,089, which is incorporated herein by reference in its entirety.) Such chimeric and humanized monoclonal antibodies can be produced by recombinant DNA techniques known in the art, for example using methods described in PCT Publication No. WO 87/02671; European Patent Application 184,187; European Patent Application 171,496; European Patent Application 173,494; PCT Publication No. WO 86/01533; U.S. Patent No. 4,816,567; European Patent Application 125,023; Better et al., 1988, Science 240:1041-1043; Liu et al., 1987, Proc. Natl. Acad. Sci. USA 84:3439-3443; Liu et al., 1987, J. Immunol. 139:3521-3526; Sun et al., 1987, Proc. Natl. Acad. Sci. USA 84:214-218; Nishimura et al., 1987, Canc. Res. 47:999-1005; Wood et al., 1985, Nature 314:446-449; and Shaw et al., 1988, J. Natl. Cancer Inst. 80:1553-1559); Morrison, 1985, Science 229:1202-1207; Oi et al., 1986, Bio/Techniques 4:214; U.S. Patent 5,225,539; Jones et al., 1986, Nature 321:552-525; Verhoeyan et al., 1988, Science 239:1534; and Beidler et al., 1988, J. Immunol. 141:4053-4060.

Completely human antibodies are particularly desirable for therapeutic treatment of human patients. Such antibodies can be produced, for example, using transgenic mice which are incapable of expressing endogenous immunoglobulin heavy and light chains genes, but which can express human heavy and light chain genes. The transgenic mice are immunized in the normal fashion with a selected antigen, e.g., all or a portion of a polypeptide of the invention. Monoclonal antibodies directed against the antigen can be obtained using conventional hybridoma technology. The human immunoglobulin transgenes harbored by the transgenic mice rearrange during B cell

differentiation, and subsequently undergo class switching and somatic mutation. Thus, using such a technique, it is possible to produce therapeutically useful IgG, IgA and IgE antibodies. For an overview of this technology for producing human antibodies, see Lonberg and Huszar, 1995, *Int. Rev. Immunol.* 13:65-93). For a detailed discussion of this technology for producing human antibodies and human monoclonal antibodies and protocols for producing such antibodies, see, e.g., U.S. Patent 5,625,126; U.S. Patent 5,633,425; U.S. Patent 5,569,825; U.S. Patent 5,661,016; and U.S. Patent 5,545,806. In addition, companies such as Abgenix, Inc. (Freemont, CA), can be engaged to provide human antibodies directed against a selected antigen using technology similar to that described above.

Completely human antibodies which recognize a selected epitope can be generated using a technique referred to as "guided selection." In this approach a selected non-human monoclonal antibody, e.g., a murine antibody, is used to guide the selection of a completely human antibody recognizing the same epitope. (Jespers et al., 1994, *Bio/technology* 12:899-903).

Antibody fragments that contain the idiotypes of the complex can be generated by techniques known in the art. For example, such fragments include, but are not limited to, the F(ab')2 fragment which can be produced by pepsin digestion of the antibody molecule; the Fab' fragment that can be generated by reducing the disulfide bridges of the F(ab')2 fragment; the Fab fragment that can be generated by treating the antibody molecular with papain and a reducing agent; and Fv fragments.

In the production of antibodies, screening for the desired antibody can be accomplished by techniques known in the art, e.g., ELISA (enzyme-linked immunosorbent assay). To select antibodies specific to a particular domain of the complex, or a derivative thereof, one may assay generated hybridomas for a product that binds to the fragment of the complex, or a derivative thereof, that contains such a domain. For selection of an antibody that specifically binds a complex of the present, or a derivative, or homologue thereof, but which does not specifically bind to the individual proteins of the complex, or a derivative, or homologue thereof, one can select on the basis of positive binding to the complex and a lack of binding to the individual protein components.

Antibodies specific to a domain of the complex, or a derivative, or homologue thereof, are also provided.

The foregoing antibodies can be used in methods known in the art relating to the localization and/or quantification of the complexes of the invention, e.g., for imaging these proteins, measuring levels thereof in appropriate physiological samples (by immunoassay), in diagnostic methods, etc. This hold true also for a derivative, or homologue thereof of a complex.

In another embodiment of the invention (see infra), an antibody to a complex or a fragment of such antibodies containing the antibody binding domain, is a therapeutic.

4.3 DIAGNOSTIC, PROGNOSTIC, AND SCREENING USES OF THE PROTEIN COMPLEXES/PROTEINS OF THE INVENTION

The particular protein complexes and proteins of the present invention may be markers of normal physiological processes, and thus have diagnostic utility. Further, definition of particular groups of patients with elevations or deficiencies of a protein complex of the present invention, or wherein the protein complex has a change in protein component composition, can lead to new nosological classifications of diseases, furthering diagnostic ability.

Examples for diseases or disorders are those as listed in table 4

Detecting levels of protein complexes, or individual component proteins that form the complexes, or detecting levels of the mRNAs encoding the components of the complex, may be used in diagnosis, prognosis, and/or staging to follow the course of a disease state, to follow a therapeutic response, etc.

A protein complex of the present invention and the individual components of the complex and a derivative, analog or subsequence thereof, encoding nucleic acids (and sequences complementary thereto), and anti-complex antibodies and antibodies directed against individual components that can form the complex, are useful in diagnostics. The foregoing molecules can be used in assays, such as immunoassays, to detect, prognose, diagnose, or monitor various conditions, diseases, and disorders characterized by aberrant levels of a complex or aberrant component composition of a complex, or monitor the treatment of such various conditions, diseases, and disorders.

In particular, such an immunoassay is carried out by a method comprising contacting a sample derived from a patient with an anti-complex antibody under conditions such that immunospecific binding can occur, and detecting or measuring the

amount of any immunospecific binding by the antibody. In a specific aspect, such binding of antibody, in tissue sections, can be used to detect aberrant complex localization, or aberrant (e.g., high, low or absent) levels of a protein complex or complexes. In a specific embodiment, an antibody to the complex can be used to assay a patient tissue or serum sample for the presence of the complex, where an aberrant level of the complex is an indication of a diseased condition. By "aberrant levels" is meant increased or decreased levels relative to that present, or a standard level representing that present, in an analogous sample from a portion or fluid of the body, or from a subject not having the disorder.

The immunoassays which can be used include but are not limited to competitive and non-competitive assay systems using techniques such as Western blots, radioimmunoassays, ELISA (enzyme linked immunosorbent assay), "sandwich" immunoassays, immunoprecipitation assays, precipitin reactions, gel diffusion precipitin reactions, immunodiffusion assays, agglutination assays, complement-fixation assays, immunoradiometric assays, fluorescent immunoassays, protein A immunoassays, to name but a few known in the art.

Nucleic acids encoding the components of the protein complex and related nucleic acid sequences and subsequences, including complementary sequences, can be used in hybridization assays. The nucleic acid sequences, or subsequences thereof, comprising about at least 8 nucleotides, can be used as hybridization probes. Hybridization assays can be used to detect, prognose, diagnose, or monitor conditions, disorders, or disease states associated with aberrant levels of the mRNAs encoding the components of a complex as described, supra. In particular, such a hybridization assay is carried out by a method comprising contacting a sample containing nucleic acid with a nucleic acid probe capable of hybridizing to component protein coding DNA or RNA, under conditions such that hybridization can occur, and detecting or measuring any resulting hybridization.

In specific embodiments, diseases and disorders involving or characterized by aberrant levels of a protein complex or aberrant complex composition can be diagnosed, or its suspected presence can be screened for, or a predisposition to develop such disorders can be detected, by determining the component protein composition of the complex, or detecting aberrant levels of a member of the complex or un-complexed component proteins or encoding nucleic acids, or functional activity including, but not restricted to, binding to an interacting partner, or by detecting mutations in component

protein RNA, DNA or protein (e.g., mutations such as translocations, truncations, changes in nucleotide or amino acid sequence relative to wild-type that cause increased or decreased expression or activity of a complex, and/or component protein).

Such diseases and disorders include, but are not limited to neurodegenerative disease such as listed in table 4.

By way of example, levels of a protein complex and the individual components of a complex can be detected by immunoassay, levels of component protein RNA or DNA can be detected by hybridization assays (e.g., Northern blots, dot blots, RNase protection assays), and binding of component proteins to each other (e.g., complex formation) can be measured by binding assays commonly known in the art. Translocations and point mutations in component protein genes can be detected by Southern blotting, RFLP analysis, PCR using primers that preferably generate a fragment spanning at least most of the gene by sequencing of genomic DNA or cDNA obtained from the patient, etc.

Assays well known in the art (e.g., assays described above such as immunoassays, nucleic acid hybridization assays, activity assays, etc.) can be used to determine whether one or more particular protein complexes are present at either increased or decreased levels, or are absent, in samples from patients suffering from a particular disease or disorder, or having a predisposition to develop such a disease or disorder, as compared to the levels in samples from subjects not having such a disease or disorder, or having a predisposition to develop such a disease or disorder. Additionally, these assays can be used to determine whether the ratio of the complex to the un-complexed components of the complex, is increased or decreased in samples from patients suffering from a particular disease or disorder, or having a predisposition to develop such a disease or disorder, as compared to the ratio in samples from subjects not having such a disease or disorder.

In the event that levels of one or more particular protein complexes (i.e., complexes formed from component protein derivatives, homologs, fragments, or analogs) are determined to be increased in patients suffering from a particular disease or disorder, or having a predisposition to develop such a disease or disorder, then the particular disease or disorder, or predisposition for a disease or disorder, can be diagnosed, have prognosis defined for, be screened for, or be monitored by detecting increased levels of the one or more protein complexes, increased levels of the mRNA

that encodes one or more members of the one or more particular protein complexes, or by detecting increased complex functional activity.

Accordingly, in a specific embodiment of the present invention, diseases and disorders involving increased levels of one or more protein complexes can be diagnosed, or their suspected presence can be screened for, or a predisposition to develop such disorders can be detected, by detecting increased levels of the one or more protein complexes, the mRNA encoding both members of the complex, or complex functional activity, or by detecting mutations in the component proteins that stabilize or enhance complex formation, e.g., mutations such as translocations in nucleic acids, truncations in the gene or protein, changes in nucleotide or amino acid sequence relative to wild-type, that stabilize or enhance complex formation.

In the event that levels of one or more particular protein complexes are determined to be decreased in patients suffering from a particular disease or disorder, or having a predisposition to develop such a disease or disorder, then the particular disease or disorder or predisposition for a disease or disorder can be diagnosed, have its prognosis determined, be screened for, or be monitored by detecting decreased levels of the one or more protein complexes, the mRNA that encodes one or more members of the particular one or more protein complexes, or by detecting decreased protein complex functional activity.

Accordingly, in a specific embodiment of the invention, diseases and disorders involving decreased levels of one or more protein complexes can be diagnosed, or their suspected presence can be screened for, or a predisposition to develop such disorders can be detected, by detecting decreased levels of the one or more protein complexes, the mRNA encoding one or more members of the one or more complexes, or complex functional activity, or by detecting mutations in the component proteins that decrease complex formation, e.g., mutations such as translocations in nucleic acids, truncations in the gene or protein, changes in nucleotide or amino acid sequence relative to wild-type, that decrease complex formation.

Accordingly, in a specific embodiment of the invention, diseases and disorders involving aberrant compositions of the complexes can be diagnosed, or their suspected presence can be screened for, or a predisposition to develop such disorders can be detected, by detecting the component proteins of one or more complexes, or the mRNA encoding the members of the one or more complexes.

The use of detection techniques, especially those involving antibodies against a protein complex, provides a method of detecting specific cells that express the complex or component proteins. Using such assays, specific cell types can be defined in which one or more particular protein complexes are expressed, and the presence of the complex or component proteins can be correlated with cell viability, state, health, etc.

Also embodied are methods to detect a protein complex of the present invention in cell culture models that express particular protein complexes or derivatives thereof, for the purpose of characterizing or preparing the complexes for harvest. This embodiment includes cell sorting of prokaryotes such as but not restricted to bacteria (Davey and Kell, 1996, *Microbiol. Rev.* 60:641-696), primary cultures and tissue specimens from eukaryotes, including mammalian species such as human (Steele et al., 1996, *Clin. Obstet. Gynecol.* 39:801-813), and continuous cell cultures (Orfao and Ruiz-Arguelles, 1996, *Clin. Biochem.* 29:5-9). Such isolations can be used as methods of diagnosis, described, supra.

In a further specific embodiment, a modulation of the formation process of a complex can be determined.

Such a modulation can either be a change in the typical time course of its formation or a change in the typical steps leading to the formation of the complete complex.

Such changes can for example be detected by analysing and comparing the process of complex formation in untreated wild type cells of a particular type and/or cells showing or having the predisposition to develop a certain disease phenotype and/or cells which have been treated with particular conditions and/or particular agents in a particular situation.

Methods to study such changes in time course are well known in the art and include for example Western-blot analysis of the proteins in the complex isolated at different steps of its formation.

Furthermore an aberrant intracellular localization of the protein complex and/or an aberrant transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or a gene dependent on the complex can serve as a marker for a disease and thus have diagnostic utility for any disease which is caused by an aberrant activity, function, composition or formation of the complex of the invention.

Methods to study the intracellular localization are well known in the art and include, but are not limited to immunofluorescence analysis using antibodies specific for components of the protein. Preferentially, double-stainings including staining of other cellular structures are being used to facilitate the detection of the intracellular localization. Methods to analyse the transcription levels of a gene dependent on the complex are also well known in the art and include Northern blot analysis, quantitative PCR etc. The abundance of proteins dependent on the protein can be analyzed as described supra. Methods to study changes in the activity of proteins dependent on complex depend on the protein. The choice of such methods will be apparent to any person skilled in the art.

4.4 THERAPEUTIC USES OF PROTEIN COMPLEXES/PROTEINS OF THE INVENTION

The present invention is directed to a method for treatment or prevention of various diseases and disorders by administration of a therapeutic compound (termed herein "therapeutic"). Such "therapeutics" include, but are not limited to, a protein complex of the present invention, the individual component proteins, and analogs and derivatives (including fragments) of the foregoing (e.g., as described hereinabove); antibodies thereto (as described hereinabove); nucleic acids encoding the component protein, and analogs or derivatives, thereof (e.g., as described hereinabove); component protein antisense nucleic acids, and agents that modulate complex formation and/or activity (i.e., agonists and antagonists).

The protein complexes as identified herein can be implicated in processes which are implicated in or associated with pathological conditions.

Diseases and disorders which can be treated and/or prevented and/or diagnosed by therapeutics interacting with any of the complexes provided herein are for example those listed in table 4.

These disorders are treated or prevented by administration of a therapeutic that modulates (i.e. inhibits or promotes) protein complex activity or formation or modulates its function or composition. Diseases or disorders associated with aberrant levels of complex activity or formation, or aberrant levels or activity of the component proteins, or aberrant complex composition or a change in the function, may be treated by

administration of a therapeutic that modulates complex formation or activity or by the administration of a protein complex.

Therapeutics may also be administered to modulate complex formation or activity or level thereof in a microbial organism such as yeast, fungi such as candida albicans causing an infectious disease in animals or humans.

Diseases and disorders characterized by increased (relative to a subject not suffering from the disease or disorder) complex levels or activity can be treated with therapeutics that antagonize (i.e., reduce or inhibit) complex formation or activity. Therapeutics that can be used include, but are not limited to, the component proteins or an analog, derivative or fragment of the component protein; anti-complex antibodies (e.g., antibodies specific for the protein complex, or a fragment or derivative of the antibody containing the binding region thereof; nucleic acids encoding the component proteins; antisense nucleic acids complementary to nucleic acids encoding the component proteins; and nucleic acids encoding the component protein that are dysfunctional due to, e.g., a heterologous insertion within the protein coding sequence, that are used to "knockout" endogenous protein function by homologous recombination, see, e.g., Capecchi, 1989, *Science* 244:1288-1292. In one embodiment, a therapeutic is 1, 2 or more antisense nucleic acids which are complementary to 1, 2, or more nucleic acids, respectfully, that encode component proteins of a complex.

In a specific embodiment of the present invention, a nucleic acid containing a portion of a component protein gene in which gene sequences flank (are both 5' and 3' to) a different gene sequence, is used as a component protein antagonist, or to promote component protein inactivation by homologous recombination (see also, Koller and Smithies, 1989, *Proc. Natl. Acad. Sci. USA* 86:8932-8935; Zijlstra et al., 1989, *Nature* 342: 435-438). Additionally, mutants or derivatives of a component protein that has greater affinity for another component protein or the complex than wild type may be administered to compete with wild type protein for binding, thereby reducing the levels of complexes containing the wild type protein. Other therapeutics that inhibit complex function can be identified by use of known convenient in vitro assays, e.g., based on their ability to inhibit complex formation, or as described in Section 4.5, infra.

In specific embodiments, therapeutics that antagonize complex formation or activity are administered therapeutically, including prophylactically, (1) in diseases or disorders involving an increased (relative to normal or desired) level of a complex, for example, in patients where complexes are overactive or overexpressed; or (2) in

diseases or disorders where an in vitro (or in vivo) assay (see infra) indicates the utility of antagonist administration. Increased levels of a complex can be readily detected, e.g., by quantifying protein and/or RNA, by obtaining a patient tissue sample (e.g., from biopsy tissue) and assaying it in vitro for RNA or protein levels, or structure and/or activity of the expressed complex (or the encoding mRNA). Many methods standard in the art can be thus employed including, but not limited to, immunoassays to detect complexes and/or visualize complexes (e.g., Western blot analysis, immunoprecipitation followed by sodium dodecyl sulfate polyacrylamide gel electrophoresis [SDS-PAGE], immunocytochemistry, etc.), and/or hybridization assays to detect concurrent expression of component protein mRNA (e.g., Northern assays, dot blot analysis, in situ hybridization, etc.).

A more specific embodiment of the present invention is directed to a method of reducing complex expression (i.e., expression of the protein components of the complex and/or formation of the complex) by targeting mRNAs that express the protein moieties. RNA therapeutics currently fall within three classes, antisense species, ribozymes, or RNA aptamers (Good et al., 1997, Gene Therapy 4:45-54).

Antisense oligonucleotides have been the most widely used. By way of example, but not limitation, antisense oligonucleotide methodology to reduce complex formation is presented below, infra. Ribozyme therapy involves the administration, induced expression, etc. of small RNA molecules with enzymatic ability to cleave, bind, or otherwise inactivate specific RNAs, to reduce or eliminate expression of particular proteins (Grassi and Marini, 1996, Annals of Medicine 28:499-510; Gibson, 1996, Cancer and Metastasis Reviews 15:287-299). RNA aptamers are specific RNA ligand proteins, such as for Tat and Rev RNA (Good et al., 1997, Gene Therapy 4:45-54) that can specifically inhibit their translation. Aptamers specific for component proteins can be identified by many methods well known in the art, for example, by affecting the formation of a complex in the protein-protein interaction assay described, infra.

In another embodiment, the activity or levels of a component protein are reduced by administration of another component protein, or the encoding nucleic acid, or an antibody that immunospecifically binds to the component protein, or a fragment or a derivative of the antibody containing the binding domain thereof.

In another aspect of the invention, diseases or disorders associated with increased levels of an component protein of the complex may be treated or prevented by administration of a therapeutic that increases complex formation if the complex formation

acts to reduce or inactivate the component protein through complex formation. Such diseases or disorders can be treated or prevented by administration of one component member of the complex, administration of antibodies or other molecules that stabilize the complex, etc.

Diseases and disorders associated with underexpression of a complex, or a component protein, are treated or prevented by administration of a therapeutic that promotes (i.e., increases or supplies) complex levels and/or function, or individual component protein function. Examples of such a therapeutic include but are not limited to a complex or a derivative, analog or fragment of the complex that are functionally active (e.g., able to form a complex), un-complexed component proteins and derivatives, analogs, and fragments of un-complexed component proteins, and nucleic acids encoding the members of a complex or functionally active derivatives or fragments of the members of the complex, e.g., for use in gene therapy. In a specific embodiment, a therapeutic includes derivatives, homologs or fragments of a component protein that increase and/or stabilize complex formation. Examples of other agonists can be identified using in vitro assays or animal models, examples of which are described, infra.

In yet other specific embodiments of the present invention, therapeutics that promote complex function are administered therapeutically, including prophylactically, (1) in diseases or disorders involving an absence or decreased (relative to normal or desired) level of a complex, for example, in patients where a complex, or the individual components necessary to form the complex, is lacking, genetically defective, biologically inactive or underactive, or under-expressed; or (2) in diseases or disorders wherein an in vitro or in vivo assay (see, infra) indicates the utility of complex agonist administration. The absence or decreased level of a complex, component protein or function can be readily detected, e.g., by obtaining a patient tissue sample (e.g., from biopsy tissue) and assaying it in vitro for RNA or protein levels, structure and/or activity of the expressed complex and/or the concurrent expression of mRNA encoding the two components of the complex. Many methods standard in the art can be thus employed, including but not limited to immunoassays to detect and/or visualize a complex, or the individual components of a complex (e.g., Western blot analysis, immunoprecipitation followed by sodium dodecyl sulfate polyacrylamide gel electrophoresis [SDS-PAGE], immunocytochemistry, etc.) and/or hybridization assays to detect expression of mRNAs encoding the individual protein components of a complex by detecting and/or visualizing

component mRNA concurrently or separately using, e.g., Northern assays, dot blot analysis, in situ hybridization, etc.

In specific embodiments, the activity or levels of a component protein are increased by administration of another component protein of the same complex, or a derivative, homolog or analog thereof, a nucleic acid encoding the other component, or an agent that stabilizes or enhances the other component, or a fragment or derivative of such an agent.

Generally, administration of products of species origin or species reactivity (in the case of antibodies) that is the same species as that of the patient is preferred. Thus, in a preferred embodiment, a human complex, or derivative, homolog or analog thereof; nucleic acids encoding the members of the human complex or a derivative, homolog or analog thereof; an antibody to a human complex, or a derivative thereof; or other human agents that affect component proteins or the complex, are therapeutically or prophylactically administered to a human patient.

Preferably, suitable in vitro or in vivo assays are utilized to determine the effect of a specific therapeutic and whether its administration is indicated for treatment of the affected tissue or individual.

In various specific embodiments, in vitro assays can be carried out with representative cells of cell types involved in a patient's disorder, to determine if a therapeutic has a desired effect upon such cell types.

Compounds for use in therapy can be tested in suitable animal model systems prior to testing in humans, including, but not limited to, rats, mice, chicken, cows, monkeys, rabbits, etc. For in vivo testing, prior to administration to humans, any animal model system known in the art may be used. Additional descriptions and sources of therapeutics that can be used according to the invention are found in Sections 4.1 to 4.3 and 4.7 herein.

4.4.1 GENE THERAPY

In a specific embodiment of the present invention, nucleic acids comprising a sequence encoding the component proteins, or a functional derivative thereof, are administered to modulate complex activity or formation by way of gene therapy. Gene therapy refers to therapy performed by the administration of a nucleic acid to a subject.

In this embodiment of the present invention, the nucleic acid expresses its encoded protein(s) that mediates a therapeutic effect by modulating complex activity or formation. Any of the methods for gene therapy available in the art can be used according to the present invention. Exemplary methods are described below.

For general reviews of the methods of gene therapy, see Goldspiel et al., 1993, Clinical Pharmacy 12:488-505; Wu and Wu, 1991, Biotherapy 3:87-95; Tolstoshev, 1993, Ann. Rev. Pharmacol. Toxicol. 32:573-596; Mulligan, 1993, Science 260:926-932; Morgan and Anderson, 1993, Ann. Rev. Biochem. 62:191-217; and May, 1993, TIBTECH 11:155-215. Methods commonly known in the art of recombinant DNA technology which can be used are described in Ausubel et al., eds., 1993, Current Protocols in Molecular Biology, John Wiley & Sons, NY; and Kriegler, 1990, Gene Transfer and Expression, A Laboratory Manual, Stockton Press, NY.

In a preferred aspect, the therapeutic comprises a nucleic acid that is part of an expression vector that expresses one or more of the component proteins, or fragments or chimeric proteins thereof, in a suitable host. In particular, such a nucleic acid has a promoter operably linked to the protein coding region(s) (or, less preferably separate promoters linked to the separate coding regions separately), said promoter being inducible or constitutive, and optionally, tissue-specific. In another particular embodiment, a nucleic acid molecule is used in which the coding sequences, and any other desired sequences, are flanked by regions that promote homologous recombination at a desired site in the genome, thus providing for intra-chromosomal expression of the component protein nucleic acids (Koller and Smithies, 1989, Proc. Natl. Acad. Sci. USA 86:8932-8935; Zijlstra et al., 1989, Nature 342:435-438).

Delivery of the nucleic acid into a patient may be either direct, in which case the patient is directly exposed to the nucleic acid or nucleic acid-carrying vector, or indirect, in which case, cells are first transformed with the nucleic acid *in vitro*, then transplanted into the patient. These two approaches are known, respectively, as *in vivo* or *ex vivo* gene therapy.

In a specific embodiment, the nucleic acid is directly administered *in vivo*, where it is expressed to produce the encoded product. This can be accomplished by any of numerous methods known in the art, e.g., by constructing it as part of an appropriate nucleic acid expression vector and administering it so that it becomes intracellular, e.g., by infection using a defective or attenuated retroviral or other viral vector (U.S. Patent No. 4,980,286), or by direct injection of naked DNA, or by use of microparticle

bombardment (e.g., a gene gun; Biostatic, Dupont), or coating with lipids or cell-surface receptors, or through use of transfecting agents, by encapsulation in liposomes, microparticles, or microcapsules, or by administering it in linkage to a peptide that is known to enter the nucleus, or by administering it in linkage to a ligand subject to receptor-mediated endocytosis that can be used to target cell types specifically expressing the receptors (e.g., Wu and Wu, 1987, *J. Biol. Chem.* 262:4429-4432), etc. In another embodiment, a nucleic acid-ligand complex can be formed in which the ligand comprises a fusogenic viral peptide that disrupts endosomes, allowing the nucleic acid to avoid lysosomal degradation. In yet another embodiment, the nucleic acid can be targeted *in vivo* for cell specific uptake and expression, by targeting a specific receptor (see, e.g., International Patent Publications WO 92/06180; WO 92/22635; WO 92/20316; WO 93/14188; and WO 93/20221. Alternatively, the nucleic acid can be introduced intracellularly and incorporated within host cell DNA for expression, by homologous recombination (Koller and Smithies, 1989, *Proc. Natl. Acad. Sci. USA* 86:8932-8935; Zijlstra et al., 1989, *Nature* 342:435-438).

In a specific embodiment, a viral vector that contains the component protein encoding nucleic acids is used. For example, a retroviral vector can be used (Miller et al., 1993, *Meth. Enzymol.* 217:581-599). These retroviral vectors have been modified to delete retroviral sequences that are not necessary for packaging of the viral genome and integration into host cell DNA. The encoding nucleic acids to be used in gene therapy is/are cloned into the vector, which facilitates delivery of the gene into a patient. More detail about retroviral vectors can be found in Boesen et al., 1994, *Biotherapy* 6:291-302, which describes the use of a retroviral vector to deliver the mdr1 gene to hematopoietic stem cells in order to make the stem cells more resistant to chemotherapy. Other references illustrating the use of retroviral vectors in gene therapy are Clowes et al., 1994, *J. Clin. Invest.* 93:644-651; Kiem et al., 1994, *Blood* 83:1467-1473; Salmons and Gunzberg, 1993, *Human Gene Therapy* 4:129-141; and Grossman and Wilson, 1993, *Curr. Opin. in Genetics and Devel.* 3:110-114.

Adenoviruses are other viral vectors that can be used in gene therapy. Adenoviruses are especially attractive vehicles for delivering genes to respiratory epithelia. Adenoviruses naturally infect respiratory epithelia where they cause a mild disease. Other targets for adenovirus-based delivery systems are the liver, the central nervous system, endothelial cells and muscle. Adenoviruses have the advantage of being capable of infecting non-dividing cells. Kozarsky and Wilson, 1993, *Curr. Opin.*

Genet. Devel. 3:499-503, discuss adenovirus-based gene therapy. The use of adenovirus vectors to transfer genes to the respiratory epithelia of rhesus monkeys has been demonstrated by Bout et al., 1994, Human Gene Therapy 5:3-10. Other instances of the use of adenoviruses in gene therapy can be found in Rosenfeld et al., 1991, Science 252:431-434; Rosenfeld et al., 1992, Cell 68:143-155; and Mastrangeli et al., 1993, J. Clin. Invest. 91:225-234.

Adeno-associated virus (AAV) has also been proposed for use in gene therapy (Walsh et al., 1993, Proc. Soc. Exp. Biol. Med. 204:289-300).

Another approach to gene therapy involves transferring a gene into cells in tissue culture by methods such as electroporation, lipofection, calcium phosphate-mediated transfection, or viral infection. Usually, the method of transfer includes the transfer of a selectable marker to the cells. The cells are then placed under selection to isolate those cells that have taken up and are expressing the transferred gene from those that have not. Those cells are then delivered to a patient.

In this embodiment, the nucleic acid is introduced into a cell prior to administration in vivo of the resulting recombinant cell. Such introduction can be carried out by any method known in the art including, but not limited to, transfection by electroporation, microinjection, infection with a viral or bacteriophage vector containing the nucleic acid sequences, cell fusion, chromosome-mediated gene transfer, microcell-mediated gene transfer, spheroplast fusion, etc. Numerous techniques are known in the art for the introduction of foreign genes into cells (see, e.g., Loeffler and Behr, 1993, Meth. Enzymol. 217:599-618; Cohen et al., 1993, Meth. Enzymol. 217:618-644; Cline, 1985, Pharmac. Ther. 29:69-92) and may be used in accordance with the present invention, provided that the necessary developmental and physiological functions of the recipient cells are not disrupted. The technique should provide for the stable transfer of the nucleic acid to the cell, so that the nucleic acid is expressible by the cell and preferably, is heritable and expressible by its cell progeny.

The resulting recombinant cells can be delivered to a patient by various methods known in the art. In a preferred embodiment, epithelial cells are injected, e.g., subcutaneously. In another embodiment, recombinant skin cells may be applied as a skin graft onto the patient. Recombinant blood cells (e.g., hematopoietic stem or progenitor cells) are preferably administered intravenously. The amount of cells envisioned for use depends on the desired effect, patient state, etc., and can be determined by one skilled in the art.

Cells into which a nucleic acid can be introduced for purposes of gene therapy encompass any desired, available cell type, and include but are not limited to epithelial cells, endothelial cells, keratinocytes, fibroblasts, muscle cells, hepatocytes, blood cells such as T lymphocytes, B lymphocytes, monocytes, macrophages, neutrophils, eosinophils, megakaryocytes, and granulocytes, various stem or progenitor cells, in particular hematopoietic stem or progenitor cells, e.g., as obtained from bone marrow, umbilical cord blood, peripheral blood, fetal liver, etc.

In a preferred embodiment, the cell used for gene therapy is autologous to the patient.

In an embodiment in which recombinant cells are used in gene therapy, a component protein encoding nucleic acid is/are introduced into the cells such that the gene or genes are expressible by the cells or their progeny, and the recombinant cells are then administered *in vivo* for therapeutic effect. In a specific embodiment, stem or progenitor cells are used. Any stem and/or progenitor cells which can be isolated and maintained *in vitro* can potentially be used in accordance with this embodiment of the present invention. Such stem cells include but are not limited to hematopoietic stem cells (HSCs), stem cells of epithelial tissues such as the skin and the lining of the gut, embryonic heart muscle cells, liver stem cells (International Patent Publication WO 94/08598), and neural stem cells (Stemple and Anderson, 1992, Cell 71:973-985).

Epithelial stem cells (ESCs), or keratinocytes, can be obtained from tissues such as the skin and the lining of the gut by known procedures (Rheinwald, 1980, Meth. Cell Biol. 2A:229). In stratified epithelial tissue such as the skin, renewal occurs by mitosis of stem cells within the germinal layer, the layer closest to the basal lamina. Similarly, stem cells within the lining of the gut provide for a rapid renewal rate of this tissue. ESCs or keratinocytes obtained from the skin or lining of the gut of a patient or donor can be grown *in tissue culture* (Rheinwald, 1980, Meth. Cell Bio. 2A:229; Pittelkow and Scott, 1986, Mayo Clinic Proc. 61:771). If the ESCs are provided by a donor, a method for suppression of host versus graft reactivity (e.g., irradiation, or drug or antibody administration to promote moderate immunosuppression) can also be used.

With respect to hematopoietic stem cells (HSCs), any technique that provides for the isolation, propagation, and maintenance *in vitro* of HSCs can be used in this embodiment of the invention. Techniques by which this may be accomplished include (a) the isolation and establishment of HSC cultures from bone marrow cells isolated from the future host, or a donor, or (b) the use of previously established long-term HSC

cultures, which may be allogeneic or xenogeneic. Non-autologous HSCs are used preferably in conjunction with a method of suppressing transplantation immune reactions between the future host and patient. In a particular embodiment of the present invention, human bone marrow cells can be obtained from the posterior iliac crest by needle aspiration (see, e.g., Kodo et al., 1984, J. Clin. Invest. 73: 1377-1384). In a preferred embodiment of the present invention, the HSCs can be made highly enriched or in substantially pure form. This enrichment can be accomplished before, during, or after long-term culturing, and can be done by any technique known in the art. Long-term cultures of bone marrow cells can be established and maintained by using, for example, modified Dexter cell culture techniques (Dexter et al., 1977, J. Cell Physiol. 91:335) or Witlock-Witte culture techniques (Witlock and Witte, 1982, Proc. Natl. Acad. Sci. USA 79:3608-3612).

In a specific embodiment, the nucleic acid to be introduced for purposes of gene therapy comprises an inducible promoter operably linked to the coding region, such that expression of the nucleic acid is controllable by controlling the presence or absence of the appropriate inducer of transcription.

Additional methods can be adapted for use to deliver a nucleic acid encoding the component proteins, or functional derivatives thereof, e.g., as described in Section 4.1, supra.

4.4.2 USE OF ANTISENSE OLIGONUCLEOTIDES FOR SUPPRESSION OF PROTEIN COMPLEX FORMATION OR PROTEIN COMPLEX/PROTEIN ACTIVITY

In a specific embodiment of the present invention, protein complex activity and formation and protein activity is inhibited by use of antisense nucleic acids for the component proteins of the complex, that inhibit transcription and/or translation of their complementary sequence. The present invention provides the therapeutic or prophylactic use of nucleic acids of at least six nucleotides that are antisense to a gene or cDNA encoding a component protein, or a portion thereof. An "antisense" nucleic acid as used herein refers to a nucleic acid capable of hybridizing to a sequence-specific portion of a component protein RNA (preferably mRNA) by virtue of some sequence complementarity. The antisense nucleic acid may be complementary to a coding and/or noncoding region of a component protein mRNA. Such antisense nucleic acids that

inhibit complex formation or activity have utility as therapeutics, and can be used in the treatment or prevention of disorders as described supra.

The antisense nucleic acids of the invention can be oligonucleotides that are double-stranded or single-stranded, RNA or DNA, or a modification or derivative thereof, which can be directly administered to a cell, or which can be produced intracellularly by transcription of exogenous, introduced sequences.

In another embodiment, the present invention is directed to a method for inhibiting the expression of component protein nucleic acid sequences, in a prokaryotic or eukaryotic cell, comprising providing the cell with an effective amount of a composition comprising an antisense nucleic acid of the component protein, or a derivative thereof, of the invention.

The antisense nucleic acids are of at least six nucleotides and are preferably oligonucleotides, ranging from 6 to about 200 nucleotides. In specific aspects, the oligonucleotide is at least 10 nucleotides, at least 15 nucleotides, at least 100 nucleotides, or at least 200 nucleotides. The oligonucleotides can be DNA or RNA or chimeric mixtures, or derivatives or modified versions thereof, and either single-stranded or double-stranded. The oligonucleotide can be modified at the base moiety, sugar moiety, or phosphate backbone. The oligonucleotide may include other appending groups such as peptides, agents facilitating transport across the cell membrane (see, e.g., Letsinger et al., 1989, Proc. Natl. Acad. Sci. USA 86:6553-6556; Lemaitre et al., 1987, Proc. Natl. Acad. Sci. USA 84:648-652; International Patent Publication No. WO 88/09810) or blood-brain barrier (see, e.g., International Patent Publication No. WO 89/10134), hybridization-triggered cleavage agents (see, e.g., Krol et al., 1988, BioTechniques 6:958-976), or intercalating agents (see, e.g., Zon, 1988, Pharm. Res. 5:539-549).

In a preferred aspect of the invention, an antisense oligonucleotide is provided, preferably as single-stranded DNA. The oligonucleotide may be modified at any position in its structure with constituents generally known in the art.

The antisense oligonucleotides may comprise at least one modified base moiety which is selected from the group including but not limited to 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xanthine, 4-acetylcytosine, 5-(carboxyhydroxymethyl)uracil, 5-carboxymethylaminomethyl-2-thio-uridine, 5-carboxymethylaminomethyluracil, dihydrouracil, β-D-galactosylqueosine, inosine, N6-isopentenyladenine, 1-methylguanine, 1-methylinosine, 2,2-dimethylguanine,

2-methyladenine, 2-methylguanine, 3-methylcytosine, 5-methylcytosine, N6-adenine, 7-methylguanine, 5-methylaminomethyluracil, 5-methoxyaminomethyl-2-thiouracil, β -D-mannosylqueosine, 5N-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methyl-thio-N6-isopentenyladenine, uracil-5-oxyacetic acid (v), wybutoxosine, pseudouracil, queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5-oxyacetic acid methylester, uracil-5-oxyacetic acid (v), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil, (acp3)w, and 2,6-diaminopurine.

In another embodiment, the oligonucleotide comprises at least one modified sugar moiety selected from the group including, but not limited to, arabinose, 2-fluoroarabinose, xylulose, and hexose.

In yet another embodiment, the oligonucleotide comprises at least one modified phosphate backbone selected from the group consisting of a phosphorothioate, a phosphorodithioate, a phosphoramidothioate, a phosphoramidate, a phosphordiamidate, a methylphosphonate, an alkyl phosphotriester, and a formacetal, or an analog of the foregoing.

In yet another embodiment, the oligonucleotide is a 2- α -anomeric oligonucleotide. An α -anomeric oligonucleotide forms specific double-stranded hybrids with complementary RNA in which, contrary to the usual β -units, the strands run parallel to each other (Gautier et al., 1987, Nucl. Acids Res. 15:6625-6641).

The oligonucleotide may be conjugated to another molecule, e.g., a peptide, hybridization-triggered cross-linking agent, transport agent, hybridization-triggered cleavage agent, etc.

Oligonucleotides of the invention may be synthesized by standard methods known in the art, e.g., by use of an automated DNA synthesizer (such as are commercially available from Biosearch, Applied Biosystems, etc.). As examples, phosphorothioate oligo-nucleotides may be synthesized by the method of Stein et al. (1988, Nucl. Acids Res. 16:3209), methylphosphonate oligonucleotides can be prepared by use of controlled pore glass polymer supports (Sarin et al., 1988, Proc. Natl. Acad. Sci. USA 85:7448-7451), etc.

In a specific embodiment, the antisense oligonucleotides comprise catalytic RNAs, or ribozymes (see, e.g., International Patent Publication No. WO 90/11364; Sarver et al., 1990, Science 247:1222-1225). In another embodiment, the oligonucleotide is a 2'-0-methylribonucleotide (Inoue et al., 1987, Nucl. Acids Res.

15:6131-6148), or a chimeric RNA-DNA analog (Inoue et al., 1987, FEBS Lett. 215:327-330).

In an alternative embodiment, the antisense nucleic acids of the invention are produced intracellularly by transcription from an exogenous sequence. For example, a vector can be introduced *in vivo* such that it is taken up by a cell, within which cell the vector or a portion thereof is transcribed, producing an antisense nucleic acid (RNA) of the invention. Such a vector would contain a sequence encoding the component protein. Such a vector can remain episomal or become chromosomally integrated, as long as it can be transcribed to produce the desired antisense RNA. Such vectors can be constructed by recombinant DNA technology methods standard in the art. Vectors can be plasmid, viral, or others known in the art to be capable of replication and expression in mammalian cells. Expression of the sequences encoding the antisense RNAs can be by any promoter known in the art to act in mammalian, preferably human, cells. Such promoters can be inducible or constitutive. Such promoters include, but are not limited to, the SV40 early promoter region (Bernoist and Chambon, 1981, Nature 290:304-310), the promoter contained in the 3' long terminal repeat of Rous sarcoma virus (Yamamoto et al., 1980, Cell 22:787-797), the herpes thymidine kinase promoter (Wagner et al., 1981, Proc. Natl. Acad. Sci. USA 78:1441-1445), the regulatory sequences of the metallothionein gene (Brinster et al., 1982, Nature 296:39-42), etc.

The antisense nucleic acids of the invention comprise a sequence complementary to at least a portion of an RNA transcript of a component protein gene, preferably a human gene. However, absolute complementarity, although preferred, is not required. A sequence "complementary to at least a portion of an RNA," as referred to herein, means a sequence having sufficient complementarity to be able to hybridize with the RNA, forming a stable duplex; in the case of double-stranded antisense nucleic acids, a single strand of the duplex DNA may thus be tested, or triplex formation may be assayed. The ability to hybridize will depend on both the degree of complementarity and the length of the antisense nucleic acid. Generally, the longer the hybridizing nucleic acid, the more base mismatches with a component protein RNA it may contain and still form a stable duplex (or triplex, as the case may be). One skilled in the art can ascertain a tolerable degree of mismatch by use of standard procedures to determine the melting point of the hybridized complex.

The component protein antisense nucleic acids can be used to treat (or prevent) disorders of a cell type that expresses, or preferably overexpresses, a protein complex.

Cell types that express or overexpress component protein RNA can be identified by various methods known in the art. Such methods include, but are not limited to, hybridization with component protein-specific nucleic acids (e.g., by Northern blot hybridization, dot blot hybridization, or *in situ* hybridization), or by observing the ability of RNA from the cell type to be translated *in vitro* into the component protein by immunohistochemistry, Western blot analysis, ELISA, etc. In a preferred aspect, primary tissue from a patient can be assayed for protein expression prior to treatment, e.g., by immunocytochemistry, *in situ* hybridization, or any number of methods to detect protein or mRNA expression.

Pharmaceutical compositions of the invention (see Section 4.7, *infra*), comprising an effective amount of a protein component antisense nucleic acid in a pharmaceutically acceptable carrier can be administered to a patient having a disease or disorder that is of a type that expresses or overexpresses a protein complex of the present invention.

The amount of antisense nucleic acid that will be effective in the treatment of a particular disorder or condition will depend on the nature of the disorder or condition, and can be determined by standard clinical techniques. Where possible, it is desirable to determine the antisense cytotoxicity *in vitro*, and then in useful animal model systems, prior to testing and use in humans.

In a specific embodiment, pharmaceutical compositions comprising antisense nucleic acids are administered via liposomes, microparticles, or microcapsules. In various embodiments of the invention, it may be useful to use such compositions to achieve sustained release of the antisense nucleic acids. In a specific embodiment, it may be desirable to utilize liposomes targeted via antibodies to specific identifiable central nervous system cell types (Leonetti et al., 1990, Proc. Natl. Acad. Sci. U.S.A. 87:2448-2451; Renneisen et al., 1990, J. Biol. Chem. 265:16337-16342).

4.5 ASSAYS OF PROTEIN COMPLEXES/PROTEINS OF THE INVENTION AND DERIVATIVES AND ANALOGS THEREOF

The functional activity of a protein complex of the present invention, or a derivative, fragment or analog thereof or protein component thereof, can be assayed by various methods. Potential modulators (e.g., agonists and antagonists) of complex

activity or formation, e.g., anti- complex antibodies and antisense nucleic acids, can be assayed for the ability to modulate complex activity or formation.

In one embodiment of the present invention, where one is assaying for the ability to bind or compete with a wild-type complex for binding to an anti-complex antibody, various immunoassays known in the art can be used, including but not limited to competitive and non-competitive assay systems using techniques such as radioimmunoassay, ELISA (enzyme linked immunosorbent assay), "sandwich" immunoassays, immunoradiometric assays, gel diffusion precipitin reactions, immunodiffusion assays, in situ immunoassays (using colloidal gold, enzyme or radioisotope labels), western blot analysis, precipitation reactions, agglutination assays (e.g., gel agglutination assays, hemagglutination assays), complement fixation assays, immunofluorescence assays, protein A assays, immunoelectrophoresis assays, etc. In one embodiment, antibody binding is detected by detecting a label on the primary antibody. In another embodiment, the primary antibody is detected by detecting binding of a secondary antibody or reagent to the primary antibody. In a further embodiment, the secondary antibody is labeled. Many means are known in the art for detecting binding in an immunoassay and are within the scope of the present invention.

The expression of the component protein genes (both endogenous and those expressed from cloned DNA containing the genes) can be detected using techniques known in the art, including but not limited to Southern hybridization (Southern, 1975, J. Mol. Biol. 98:503-517), northern hybridization (see, e.g., Freeman et al., 1983, Proc. Natl. Acad. Sci. USA 80:4094-4098), restriction endonuclease mapping (Sambrook et al., 1989, Molecular Cloning, A Laboratory Manual, 2nd Ed. Cold Spring Harbor Laboratory Press, New York), RNase protection assays (Current Protocols in Molecular Biology, John Wiley and Sons, New York, 1997), DNA sequence analysis, and polymerase chain reaction amplification (PCR; U.S. Patent Nos. 4,683,202, 4,683,195, and 4,889,818; Gyllenstein et al., 1988, Proc. Natl. Acad. Sci. USA 85:7652-7657; Ochman et al., 1988, Genetics 120:621-623; Loh et al., 1989, Science 243:217-220) followed by Southern hybridization with probes specific for the component protein genes, in various cell types. Methods of amplification other than PCR commonly known in the art can be employed. In one embodiment, Southern hybridization can be used to detect genetic linkage of component protein gene mutations to physiological or pathological states. Various cell types, at various stages of development, can be characterized for their expression of component proteins at the same time and in the same cells. The stringency of the

hybridization conditions for northern or Southern blot analysis can be manipulated to ensure detection of nucleic acids with the desired degree of relatedness to the specific probes used. Modifications to these methods and other methods commonly known in the art can be used.

Derivatives (e.g., fragments), homologs and analogs of one component protein can be assayed for binding to another component protein in the same complex by any method known in the art, for example the modified yeast matrix mating test described in Section 4.6.1 infra, immunoprecipitation with an antibody that binds to the component protein complexed with other component proteins in the same complex, followed by size fractionation of the immunoprecipitated proteins (e.g., by denaturing or nondenaturing polyacrylamide gel electrophoresis), Western blot analysis, etc.

One embodiment of the invention provides a method for screening a derivative, homolog or analog of a component protein for biological activity comprising contacting said derivative, homolog or analog of the component protein with the other component proteins in the same complex; and detecting the formation of a complex between said derivative, homolog or analog of the component protein and the other component proteins; wherein detecting formation of said complex indicates that said derivative, homolog or analog of has biological (e.g., binding) activity.

The invention also provides methods of modulating the activity of a component protein that can participate in a protein complex by administration of a binding partner of that protein or derivative, homolog or analog thereof.

In a specific embodiment of the present invention, a protein complex of the present invention is administered to treat or prevent a disease or disorder, since the complex and/or component proteins have been implicated in the disease and disorder. Accordingly, a protein complex or a derivative, homolog, analog or fragment thereof, nucleic acids encoding the component proteins, anti-complex antibodies, and other modulators of protein complex activity, can be tested for activity in treating or preventing a disease or disorder in in vitro and in vivo assays.

In one embodiment, a therapeutic of the invention can be assayed for activity in treating or preventing a disease by contacting cultured cells that exhibit an indicator of the disease in vitro, with the therapeutic, and comparing the level of said indicator in the cells contacted with the therapeutic, with said level of said indicator in cells not so contacted, wherein a lower level in said contacted cells indicates that the therapeutic has activity in treating or preventing the disease.

In another embodiment of the invention, a therapeutic of the invention can be assayed for activity in treating or preventing a disease by administering the therapeutic to a test animal that is predisposed to develop symptoms of a disease, and measuring the change in said symptoms of the disease after administration of said therapeutic, wherein a reduction in the severity of the symptoms of the disease or prevention of the symptoms of the disease indicates that the therapeutic has activity in treating or preventing the disease. Such a test animal can be any one of a number of animal models known in the art for disease. These animal models are well known in the art. These animal models include, but are not limited to those which are listed in the section 4.6 (supra) as exemplary animal models to study any of the complexes provided in the invention.

4.6 SCREENING FOR MODULATORS OF THE PROTEIN COMPLEXES/PROTEINS OF THE INVENTION

A complex of the present invention, the component proteins of the complex and nucleic acids encoding the component proteins, as well as derivatives and fragments of the amino and nucleic acids, can be used to screen for compounds that bind to, or modulate the amount of, activity of, or protein component composition of, said complex, and thus, have potential use as modulators, i.e., agonists or antagonists, of complex activity, and/or complex formation, i.e., the amount of complex formed, and/or protein component composition of the complex.

Thus, the present invention is also directed to methods for screening for molecules that bind to, or modulate the function of, amount of, activity of, formation of or protein component composition of, a complex of the present invention. In one embodiment of the invention, the method for screening for a molecule that modulates directly or indirectly the function, activity or formation of a complex of the present invention comprises exposing said complex, or a cell or organism containing the complex machinery, to one or more candidate molecules under conditions conducive to modulation; and determining the amount of, the biochemical activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate

molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

In a further specific embodiment, a modulation of the formation process of a complex can be determined.

Such a modulation can either be a change in the typical time course of its formation or a change in the typical steps leading to the formation of the complete complex.

Such changes can for example be detected by analysing and comparing the process of complex formation in untreated wild type cells of a particular type and/or cells showing or having the predisposition to develop a certain disease phenotype and/or cells which have been treated with particular conditions and/or particular agents in a particular situation. Methods to study such changes in time course are well known in the art and include for example Western-blot analysis of the proteins in the complex isolated at different steps of its formation.

Furthermore an aberrant intracellular localization of the protein complex and/or an aberrant transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or a gene dependent on the complex can serve as a marker for a disease and thus have diagnostic utility for any disease which is caused by an aberrant activity, function, composition or formation of the complex of the invention.

Methods to study the intracellular localization are well known in the art and include, but are not limited to immunofluorescence analysis using antibodies specific for components of the protein. Preferentially, double-stainings including staining of other cellular structures are being used to facilitate the detection of the intracellular localization. Methods to analyse the transcription levels of a gene dependent on the complex are also well known in the art and include Northern blot analysis, quantitative PCR etc. The abundance of proteins dependent on the protein can be analyzed as described supra. Methods to study changes in the activity of proteins dependent on complex depend on the protein. The choice of such methods will be apparent to any person skilled in the art.

In another embodiment, the present invention further relates to a process for the identification and/or preparation of an effector of the complex comprising the step of bringing into contact a product of any of claims 1 to 8 with a compound, a mixture or a library of compounds and determining whether the compound or a certain compound of the mixture or library binds to the product and/or effects the products biological activity and optionally further purifying the compound positively tested as effector.

In another embodiment, the present invention is directed to a method for screening for a molecule that binds a protein complex of the present invention comprising exposing said complex, or a cell or organism containing the complex machinery, to one or more candidate molecules; and determining whether said complex is bound by any of said candidate molecules. Such screening assays can be carried out using cell-free and cell-based methods that are commonly known in the art in vitro, in vivo or ex vivo. For example, an isolated complex can be employed, or a cell can be contacted with the candidate molecule and the complex can be isolated from such contacted cells and the isolated complex can be assayed for activity or component composition. In another example, a cell containing the complex can be contacted with the candidate molecule and the levels of the complex in the contacted cell can be measured. Additionally, such assays can be carried out in cells recombinantly expressing a component protein from the fourth column of table 1, or a functionally active fragment or functionally active derivative thereof, and a component protein from fifth column of table 1, or a functionally active fragment or functionally active derivative thereof. Additionally, such assays can also be carried out in cells recombinantly expressing all component proteins from the group of proteins in the fifth column of table 1.

For example, assays can be carried out using recombinant cells expressing the protein components of a complex, to screen for molecules that bind to, or interfere with, or promote complex activity or formation. In preferred embodiments, polypeptide derivatives that have superior stabilities but retain the ability to form a complex (e.g., one or more component proteins modified to be resistant to proteolytic degradation in the binding assay buffers, or to be resistant to oxidative degradation), are used to screen for modulators of complex activity or formation. Such resistant molecules can be generated, e.g., by substitution of amino acids at proteolytic cleavage sites, the use of chemically derivatized amino acids at proteolytic susceptible sites, and the replacement of amino acid residues subject to oxidation, i.e. methionine and cysteine.

A particular aspect of the present invention relates to identifying molecules that inhibit or promote formation or degradation of a complex of the present invention, e.g., using the method described for isolating the complex and identifying members of the complex using the TAP assay described in Section 4, infra, and in WO 00/09716 and Rigaut et al., 1999, *Nature Biotechnol.* 17:1030-1032, which are each incorporated by reference in their entirety. TNRF1

In another embodiment of the invention, a modulator is identified by administering a candidate molecule to a transgenic non-human animal expressing the complex component proteins from promoters that are not the native promoters of the respective proteins, more preferably where the candidate molecule is also recombinantly expressed in the transgenic non-human animal. Alternatively, the method for identifying such a modulator can be carried out in vitro, preferably with a purified complex, and a purified candidate molecule.

Agents/molecules (candidate molecules) to be screened can be provided as mixtures of a limited number of specified compounds, or as compound libraries, peptide libraries and the like. Agents/molecules to be screened may also include all forms of antisera, antisense nucleic acids, etc., that can modulate complex activity or formation. Exemplary candidate molecules and libraries for screening are set forth in Section 4.6.1, infra.

Screening the libraries can be accomplished by any of a variety of commonly known methods. See, e.g., the following references, which disclose screening of peptide libraries: Parmley and Smith, 1989, *Adv. Exp. Med. Biol.* 251:215-218; Scott and Smith, 1990, *Science* 249:386-390; Fowlkes et al., 1992, *BioTechniques* 13:422-427; Oldenburg et al., 1992, *Proc. Natl. Acad. Sci. USA* 89:5393-5397; Yu et al., 1994, *Cell* 76:933-945; Staudt et al., 1988, *Science* 241:577-580; Bock et al., 1992, *Nature* 355:564-566; Tuerk et al., 1992, *Proc. Natl. Acad. Sci. USA* 89:6988-6992; Ellington et al., 1992, *Nature* 355:850-852; U.S. Patent No. 5,096,815, U.S. Patent No. 5,223,409, and U.S. Patent No. 5,198,346, all to Ladner et al.; Rebar and Pabo, 1993, *Science* 263:671-673; and International Patent Publication No. WO 94/18318.

In a specific embodiment, screening can be carried out by contacting the library members with a complex immobilized on a solid phase, and harvesting those library members that bind to the protein (or encoding nucleic acid or derivative). Examples of such screening methods, termed "panning" techniques, are described by way of example in Parmley and Smith, 1988, *Gene* 73:305-318; Fowlkes et al., 1992, *BioTechniques*

13:422-427; International Patent Publication No. WO 94/18318; and in references cited hereinabove.

In a specific embodiment, fragments and/or analogs of protein components of a complex, especially peptidomimetics, are screened for activity as competitive or non-competitive inhibitors of complex formation (amount of complex or composition of complex) or activity in the cell, which thereby inhibit complex activity or formation in the cell.

In one embodiment, agents that modulate (i.e., antagonize or agonize) complex activity or formation can be screened for using a binding inhibition assay, wherein agents are screened for their ability to modulate formation of a complex under aqueous, or physiological, binding conditions in which complex formation occurs in the absence of the agent to be tested. Agents that interfere with the formation of complexes of the invention are identified as antagonists of complex formation. Agents that promote the formation of complexes are identified as agonists of complex formation. Agents that completely block the formation of complexes are identified as inhibitors of complex formation.

Methods for screening may involve labeling the component proteins of the complex with radioligands (e.g., ^{125}I or ^3H), magnetic ligands (e.g., paramagnetic beads covalently attached to photobiotin acetate), fluorescent ligands (e.g., fluorescein or rhodamine), or enzyme ligands (e.g., luciferase or β -galactosidase). The reactants that bind in solution can then be isolated by one of many techniques known in the art, including but not restricted to, co-immunoprecipitation of the labeled complex moiety using antisera against the unlabeled binding partner (or labeled binding partner with a distinguishable marker from that used on the second labeled complex moiety), immunoaffinity chromatography, size exclusion chromatography, and gradient density centrifugation. In a preferred embodiment, the labeled binding partner is a small fragment or peptidomimetic that is not retained by a commercially available filter. Upon binding, the labeled species is then unable to pass through the filter, providing for a simple assay of complex formation.

Methods commonly known in the art are used to label at least one of the component members of the complex. Suitable labeling methods include, but are not limited to, radiolabeling by incorporation of radiolabeled amino acids, e.g., ^3H -leucine or ^{35}S -methionine, radiolabeling by post-translational iodination with ^{125}I or ^{131}I using the chloramine T method, Bolton-Hunter reagents, etc., or labeling with ^{32}P using phosphorylase and inorganic radiolabeled phosphorous, biotin labeling with photobiotin-

acetate and sunlamp exposure, etc. In cases where one of the members of the complex is immobilized, e.g., as described infra, the free species is labeled. Where neither of the interacting species is immobilized, each can be labeled with a distinguishable marker such that isolation of both moieties can be followed to provide for more accurate quantification, and to distinguish the formation of homomeric from heteromeric complexes. Methods that utilize accessory proteins that bind to one of the modified interactants to improve the sensitivity of detection, increase the stability of the complex, etc., are provided.

Typical binding conditions are, for example, but not by way of limitation, in an aqueous salt solution of 10-250 mM NaCl, 5-50 mM Tris-HCl, pH 5-8, and 0.5% Triton X-100 or other detergent that improves specificity of interaction. Metal chelators and/or divalent cations may be added to improve binding and/or reduce proteolysis. Reaction temperatures may include 4, 10, 15, 22, 25, 35, or 42 degrees Celsius, and time of incubation is typically at least 15 seconds, but longer times are preferred to allow binding equilibrium to occur. Particular complexes can be assayed using routine protein binding assays to determine optimal binding conditions for reproducible binding.

The physical parameters of complex formation can be analyzed by quantification of complex formation using assay methods specific for the label used, e.g., liquid scintillation counting for radioactivity detection, enzyme activity for enzyme-labeled moieties, etc. The reaction results are then analyzed utilizing Scatchard analysis, Hill analysis, and other methods commonly known in the arts (see, e.g., Proteins, Structures, and Molecular Principles, 2nd Edition (1993) Creighton, Ed., W.H. Freeman and Company, New York).

In a second common approach to binding assays, one of the binding species is immobilized on a filter, in a microtiter plate well, in a test tube, to a chromatography matrix, etc., either covalently or non-covalently. Proteins can be covalently immobilized using any method well known in the art, for example, but not limited to the method of Kadonaga and Tjian, 1986, Proc. Natl. Acad. Sci. USA 83:5889-5893, i.e., linkage to a cyanogen-bromide derivatized substrate such as CNBr-Sepharose 4B (Pharmacia). Where needed, the use of spacers can reduce steric hindrance by the substrate. Non-covalent attachment of proteins to a substrate include, but are not limited to, attachment of a protein to a charged surface, binding with specific antibodies, binding to a third unrelated interacting protein, etc.

Assays of agents (including cell extracts or a library pool) for competition for binding of one member of a complex (or derivatives thereof) with another member of the complex labeled by any means (e.g., those means described above) are provided to screen for competitors or enhancers of complex formation.

In specific embodiments, blocking agents to inhibit non-specific binding of reagents to other protein components, or absorptive losses of reagents to plastics, immobilization matrices, etc., are included in the assay mixture. Blocking agents include, but are not restricted to bovine serum albumin, β -casein, nonfat dried milk, Denhardt's reagent, Ficoll, polyvinylpyrrolidine, nonionic detergents (NP40, Triton X-100, Tween 20, Tween 80, etc.), ionic detergents (e.g., SDS, LDS, etc.), polyethylene glycol, etc. Appropriate blocking agent concentrations allow complex formation.

After binding is performed, unbound, labeled protein is removed in the supernatant, and the immobilized protein retaining any bound, labeled protein is washed extensively. The amount of bound label is then quantified using standard methods in the art to detect the label as described, *supra*.

In another specific embodiment screening for modulators of the protein complexes/protein as provided herein can be carried out by attaching those and/or the antibodies as provided herein to a solid carrier. In a further specific embodiment, the invention relates to an array of said molecules.

The preparation of such an array containing different types of proteins, including antibodies) is well known in the art and is apparent to a person skilled in the art (see e.g. Ekins et al., 1989, *J. Pharm. Biomed. Anal.* 7:155-168; Mitchell et al. 2002, *Nature Biotechnol.* 20:225-229; Petricoin et al., 2002, *Lancet* 359:572-577; Templin et al., 2001, *Trends Biotechnol.* 20:160-166; Wilson and Nock, 2001, *Curr. Opin. Chem. Biol.* 6:81-85; Lee et al., 2002 *Science* 295:1702-1705; MacBeath and Schreiber, 2000, *Science* 289:1760; Blawas and Reichert, 1998, *Biomaterials* 19:595; Kane et al., 1999, *Biomaterials* 20:2363; Chen et al., 1997, *Science* 276:1425; Vaughan et al., 1996, *Nature Biotechnol.* 14:309-314; Mahler et al., 1997, *Immunotechnology* 3:31-43; Roberts et al., 1999, *Curr. Opin. Chem. Biol.* 3:268-273; Nord et al., 1997, *Nature Biotechnol.* 15:772-777; Nord et al., 2001, *Eur. J. Biochem.* 268:4269-4277; Brody and Gold, 2000, *Rev. Mol. Biotechnol.* 74:5-13; Karlstrom and Nygren, 2001, *Anal. Biochem.* 295:22-30; Nelson et al., 2000, *Electrophoresis* 21:1155-1163; Honore et al., 2001, *Expert Rev. Mol. Diagn.* 3:265-274; Albala, 2001, *Expert Rev. Mol. Diagn.* 2:145-152, Figeys and Pinto, 2001, *Electrophoresis* 2:208-216 and references in the publications listed here).

Complexes can be attached to an array by different means as will be apparent to a person skilled in the art. Complexes can for example be added to the array via a TAP-tag (as described in WO/0009716 and in Rigaut et al., 1999, Nature Biotechnol. 10:1030-1032) after the purification step or by another suitable purification scheme as will be apparent to a person skilled in the art.

Optionally, the proteins of the complex can be cross-linked to enhance the stability of the complex. Different methods to cross-link proteins are well known in the art. Reactive end-groups of cross-linking agents include but are not limited to -COOH, -SH, -NH₂ or N-oxy-succinamate.

The spacer of the cross-linking agent should be chosen with respect to the size of the complex to be cross-linked. For small protein complexes, comprising only a few proteins, relatively short spacers are preferable in order to reduce the likelihood of cross-linking separate complexes in the reaction mixture. For larger protein complexes, additional use of larger spacers is preferable in order to facilitate cross-linking between proteins within the complex.

It is preferable to check the success-rate of cross-linking before linking the complex to the carrier.

As will be apparent to a person skilled in the art, the optimal rate of cross-linking need to be determined on a case by case basis. This can be achieved by methods well known in the art, some of which are exemplary described below.

A sufficient rate of cross-linking can be checked f.e. by analysing the cross-linked complex vs. a non-cross-linked complex on a denaturing protein gel. If cross-linking has been performed successfully, the proteins of the complex are expected to be found in the same lane, whereas the proteins of the non-cross-linked complex are expected to be separated according to their individual characteristics. Optionally the presence of all proteins of the complex can be further checked by peptide-sequencing of proteins in the respective bands using methods well known in the art such as mass spectrometry and/or Edman degradation.

In addition, a rate of crosslinking which is too high should also be avoided. If cross-linking has been carried out too extensively, there will be an increasing amount of cross-linking of the individual protein complex, which potentially interferes with a screening for potential binding partners and/or modulators etc. using the arrays.

The presence of such structures can be determined by methods well known in the art and include e.g. gel-filtration experiments comparing the gel filtration profile solutions containing cross-linked complexes vs. uncross-linked complexes.

Optionally, functional assays as will be apparent to a person skilled in the art, some of which are exemplarily provided herein, can be performed to check the integrity of the complex.

Alternatively, members of the protein complex can be expressed as a single fusion protein and coupled to the matrix as will be apparent to a person skilled in the art.

Optionally, the attachment of the complex or proteins or antibody as outlined above can be further monitored by various methods apparent to a person skilled in the art. Those include, but are not limited to surface plasmon resonance (see e.g. McDonnel, 2001, Curr. Opin. Chem. Biol. 5:572-577; Lee, 2001, Trends Biotechnol. 19:217-222; Weinberger et al., 2000, 1:395-416; Pearson et al., 2000, Ann. Clin. Biochem. 37:119-145; Vely et al., 2000, Methods Mol. Biol. 121:313-321; Slepak, 2000, J. Mol Recognit. 13:20-26.

Exemplary assays useful for measuring the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the mDAB1-complex include but are not limited to those described in Vassar R et al., 1999, Science, 286:735-41.

Exemplary assays useful for measuring the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the mDAB1-complex include but are not limited to those described in Yan R et al., 1999, Nature, 402:533-7.

Exemplary assays useful for measuring the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting of the mDAB1-complex include but are not limited to those described in Tian Gaochao et al., 2002, J Biol Chem, 277:31499-505.

Exemplary assays useful for measuring transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the mDAB1-complex include but are not limited to those described in Cao X et al., 2001, Science, 293:115-20.

Exemplary assays useful for measuring transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the JIP1-complex include but are not limited to those described in Cao X et al., 2001, Science, 293:115-20.

Exemplary assays useful for measuring the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the JIP1-complex include but are not limited to those described in Vassar R et al., 1999, Science, 286:735-41.

Exemplary assays useful for measuring the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the JIP1-complex include but are not limited to those described in Yan R et al., 1999, Nature, 402:533-7.

Exemplary assays useful for measuring the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the JIP1-complex include but are not limited to those described in Tian Gaochao et al., 2002, J Biol Chem, 277:31499-505.

Exemplary assays useful for measuring transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Fe65L2-complex include but are not limited to those described in Cao X et al., 2001, Science, 293:115-20.

Exemplary assays useful for measuring the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting

protein(s)) of the Fe65L2-complex include but are not limited to those described in Vassar R et al., 1999, Science, 286:735-41.

Exemplary assays useful for measuring the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Fe65L2-complex include but are not limited to those described in Yan R et al., 1999, Nature, 402:533-7.

Exemplary assays useful for measuring the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting of the Fe65L2-complex include but are not limited to those described in Tian Gaochao et al., 2002, J Biol Chem, 277:31499-505.

Exemplary assays useful for measuring the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Pilt/TJP4-complex include but are not limited to those described in Vassar R et al., 1999, Science, 286:735-41.

Exemplary assays useful for measuring the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Pilt/TJP4-complex include but are not limited to those described in Yan R et al., 1999, Nature, 402:533-7.

Exemplary assays useful for measuring the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting of the Pilt/TJP4-complex include but are not limited to those described in Tian Gaochao et al., 2002, J Biol Chem, 277:31499-505.

Exemplary assays useful for measuring transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Pilt/TJP4-complex include but are not limited to those described in Cao X et al., 2001, Science, 293:115-20.

Exemplary assays useful for measuring the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting

proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s) of the Neurotrypsin-complex include but are not limited to those described in Vassar R et al., 1999, Science, 286:735-41.

Exemplary assays useful for measuring the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s) of the Neurotrypsin-complex include but are not limited to those described in Yan R et al., 1999, Nature, 402:533-7.

Exemplary assays useful for measuring the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s) of the Neurotrypsin-complex include but are not limited to those described in Tian Gaochao et al., 2002, J Biol Chem, 277:31499-505.

Exemplary assays useful for measuring transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s) of the Hunc18a-complex include but are not limited to those described in Cao X et al., 2001, Science, 293:115-20.

Exemplary assays useful for measuring the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s) of the Hunc18a-complex include but are not limited to those described in Vassar R et al., 1999, Science, 286:735-41.

Exemplary assays useful for measuring the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s) of the Hunc18a-complex include but are not limited to those described in Yan R et al., 1999, Nature, 402:533-7.

Exemplary assays useful for measuring the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s) of the Hunc18a-complex include but are not limited to those described in Tian Gaochao et al., 2002, J Biol Chem, 277:31499-505.

Exemplary assays useful for measuring the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Telencephalin-complex include but are not limited to those described in Vassar R et al., 1999, Science, 286:735-41.

Exemplary assays useful for measuring the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Telencephalin-complex include but are not limited to those described in Yan R et al., 1999, Nature, 402:533-7.

Exemplary assays useful for measuring the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Telencephalin-complex include but are not limited to those described in Tian Gaochao et al., 2002, J Biol Chem, 277:31499-505.

Exemplary assays useful for measuring transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Telencephalin-complex include but are not limited to those described in Cao X et al., 2001, Science, 293:115-20.

Exemplary assays useful for measuring the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the PC7-complex include but are not limited to those described in Vassar R et al., 1999, Science, 286:735-41.

Exemplary assays useful for measuring the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the PC7-complex include but are not limited to those described in Yan R et al., 1999, Nature, 402:533-7.

Exemplary assays useful for measuring the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA)

and/or plasmids encoding the interacting of the PC7-complex include but are not limited to those described in Tian Gaochao et al., 2002, J Biol Chem, 277:31499-505.

Exemplary assays useful for measuring transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the PC7-complex include but are not limited to those described in Cao X et al., 2001, Science, 293:115-20.

Exemplary assays useful for measuring the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the VTRP-complex include but are not limited to those described in Vassar R et al., 1999, Science, 286:735-41.

Exemplary assays useful for measuring the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the VTRP-complex include but are not limited to those described in Yan R et al., 1999, Nature, 402:533-7.

Exemplary assays useful for measuring the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting of the VTRP-complex include but are not limited to those described in Tian Gaochao et al., 2002, J Biol Chem, 277:31499-505.

Exemplary assays useful for measuring transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the VTRP-complex include but are not limited to those described in Cao X et al., 2001, Science, 293:115-20.

Exemplary assays useful for measuring the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the BACE1 (new)-complex include but are not limited to those described in Vassar R et al., 1999, Science, 286:735-41.

Exemplary assays useful for measuring the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the

expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the BACE1 (new)-complex include but are not limited to those described in Yan R et al., 1999, Nature, 402:533-7.

Exemplary assays useful for measuring the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting of the BACE1 (new)-complex include but are not limited to those described in Tian Gaochao et al., 2002, J Biol Chem, 277:31499-505.

Exemplary assays useful for measuring transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the BACE1 (new)-complex include but are not limited to those described in Cao X et al., 2001, Science, 293:115-20.

Exemplary assays useful for measuring transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the BACE2-complex include but are not limited to those described in Cao X et al., 2001, Science, 293:115-20.

Exemplary assays useful for measuring the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the BACE2-complex include but are not limited to those described in Vassar R et al., 1999, Science, 286:735-41.

Exemplary assays useful for measuring the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the BACE2-complex include but are not limited to those described in Yan R et al., 1999, Nature, 402:533-7.

Exemplary assays useful for measuring the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting of the BACE2-complex include but are not limited to those described in Tian Gaochao et al., 2002, J Biol Chem, 277:31499-505.

Exemplary assays useful for measuring transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the PALADIN-complex include but are not limited to those described in Cao X et al., 2001, Science, 293:115-20.

Exemplary assays useful for measuring the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the PALADIN-complex include but are not limited to those described in Vassar R et al., 1999, Science, 286:735-41.

Exemplary assays useful for measuring the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the PALADIN-complex include but are not limited to those described in Yan R et al., 1999, Nature, 402:533-7.

Exemplary assays useful for measuring the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the PALADIN-complex include but are not limited to those described in Tian Gaochao et al., 2002, J Biol Chem, 277:31499-505.

Exemplary assays useful for measuring transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the TFCP2-complex include but are not limited to those described in Cao X et al., 2001, Science, 293:115-20.

Exemplary assays useful for measuring the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the p75 NTR-complex include but are not limited to those described in Vassar R et al., 1999, Science, 286:735-41.

Exemplary assays useful for measuring the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA)

and/or plasmids encoding the interacting protein(s)) of the p75 NTR-complex include but are not limited to those described in Yan R et al., 1999, Nature, 402:533-7.

Exemplary assays useful for measuring the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting of the p75 NTR-complex include but are not limited to those described in Tian Gaochao et al., 2002, J Biol Chem, 277:31499-505.

Exemplary assays useful for measuring transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the p75 NTR-complex include but are not limited to those described in Cao X et al., 2001, Science, 293:115-20.

Exemplary assays useful for measuring the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Lamezin-complex include but are not limited to those described in Vassar R et al., 1999, Science, 286:735-41.

Exemplary assays useful for measuring the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Lamezin-complex include but are not limited to those described in Yan R et al., 1999, Nature, 402:533-7.

Exemplary assays useful for measuring the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting of the Lamezin-complex include but are not limited to those described in Tian Gaochao et al., 2002, J Biol Chem, 277:31499-505.

Exemplary assays useful for measuring transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Lamezin-complex include but are not limited to those described in Cao X et al., 2001, Science, 293:115-20.

Exemplary assays useful for measuring transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by

means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the APP-C59-complex include but are not limited to those described in Cao X et al., 2001, Science, 293:115-20.

Exemplary assays useful for measuring the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the BRI/ITM2B-complex include but are not limited to those described in Vassar R et al., 1999, Science, 286:735-41.

Exemplary assays useful for measuring the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the BRI/ITM2B-complex include but are not limited to those described in Yan R et al., 1999, Nature, 402:533-7.

Exemplary assays useful for measuring the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the BRI/ITM2B-complex include but are not limited to those described in Tian Gaochao et al., 2002, J Biol Chem, 277:31499-505.

Exemplary assays useful for measuring transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the BRI/ITM2B-complex include but are not limited to those described in Cao X et al., 2001, Science, 293:115-20.

4.6.1 CANDIDATE MOLECULES

Any molecule known in the art can be tested for its ability to modulate (increase or decrease) the amount of, activity of, or protein component composition of a complex of the present invention as detected by a change in the amount of, activity of, or protein component composition of, said complex. By way of example, a change in the amount of the complex can be detected by detecting a change in the amount of the complex that can be isolated from a cell expressing the complex machinery. For identifying a molecule that modulates complex activity, candidate molecules can be directly provided

to a cell expressing the complex machinery, or, in the case of candidate proteins, can be provided by providing their encoding nucleic acids under conditions in which the nucleic acids are recombinantly expressed to produce the candidate proteins within the cell expressing the complex machinery, the complex is then isolated from the cell and the isolated complex is assayed for activity using methods well known in the art, not limited to those described, *supra*.

This embodiment of the invention is well suited to screen chemical libraries for molecules which modulate, e.g., inhibit, antagonize, or agonize, the amount of, activity of, or protein component composition of the complex. The chemical libraries can be peptide libraries, peptidomimetic libraries, chemically synthesized libraries, recombinant, e.g., phage display libraries, and in vitro translation-based libraries, other non-peptide synthetic organic libraries, etc.

Exemplary libraries are commercially available from several sources (ArQule, Tripos/PanLabs, ChemDesign, Pharmacopoeia). In some cases, these chemical libraries are generated using combinatorial strategies that encode the identity of each member of the library on a substrate to which the member compound is attached, thus allowing direct and immediate identification of a molecule that is an effective modulator. Thus, in many combinatorial approaches, the position on a plate of a compound specifies that compound's composition. Also, in one example, a single plate position may have from 1-20 chemicals that can be screened by administration to a well containing the interactions of interest. Thus, if modulation is detected, smaller and smaller pools of interacting pairs can be assayed for the modulation activity. By such methods, many candidate molecules can be screened.

Many diversity libraries suitable for use are known in the art and can be used to provide compounds to be tested according to the present invention. Alternatively, libraries can be constructed using standard methods. Chemical (synthetic) libraries, recombinant expression libraries, or polysome-based libraries are exemplary types of libraries that can be used.

The libraries can be constrained or semirigid (having some degree of structural rigidity), or linear or nonconstrained. The library can be a cDNA or genomic expression library, random peptide expression library or a chemically synthesized random peptide library, or non-peptide library. Expression libraries are introduced into the cells in which the assay occurs, where the nucleic acids of the library are expressed to produce their encoded proteins.

In one embodiment, peptide libraries that can be used in the present invention may be libraries that are chemically synthesized in vitro. Examples of such libraries are given in Houghten et al., 1991, *Nature* 354:84-86, which describes mixtures of free hexapeptides in which the first and second residues in each peptide were individually and specifically defined; Lam et al., 1991, *Nature* 354:82-84, which describes a "one bead, one peptide" approach in which a solid phase split synthesis scheme produced a library of peptides in which each bead in the collection had immobilized thereon a single, random sequence of amino acid residues; Medynski, 1994, *Bio/Technology* 12:709-710, which describes split synthesis and T-bag synthesis methods; and Gallop et al., 1994, *J. Med. Chem.* 37:1233-1251. Simply by way of other examples, a combinatorial library may be prepared for use, according to the methods of Ohlmeyer et al., 1993, *Proc. Natl. Acad. Sci. USA* 90:10922-10926; Erb et al., 1994, *Proc. Natl. Acad. Sci. USA* 91:11422-11426; Houghten et al., 1992, *Biotechniques* 13:412; Jayawickreme et al., 1994, *Proc. Natl. Acad. Sci. USA* 91:1614-1618; or Salmon et al., 1993, *Proc. Natl. Acad. Sci. USA* 90:11708-11712. PCT Publication No. WO 93/20242 and Brenner and Lerner, 1992, *Proc. Natl. Acad. Sci. USA* 89:5381-5383 describe "encoded combinatorial chemical libraries," that contain oligonucleotide identifiers for each chemical polymer library member.

In a preferred embodiment, the library screened is a biological expression library that is a random peptide phage display library, where the random peptides are constrained (e.g., by virtue of having disulfide bonding).

Further, more general, structurally constrained, organic diversity (e.g., nonpeptide) libraries, can also be used. By way of example, a benzodiazepine library (see e.g., Bunin et al., 1994, *Proc. Natl. Acad. Sci. USA* 91:4708-4712) may be used.

Conformationally constrained libraries that can be used include but are not limited to those containing invariant cysteine residues which, in an oxidizing environment, cross-link by disulfide bonds to form cystines, modified peptides (e.g., incorporating fluorine, metals, isotopic labels, are phosphorylated, etc.), peptides containing one or more non-naturally occurring amino acids, non-peptide structures, and peptides containing a significant fraction of -carboxyglutamic acid.

Libraries of non-peptides, e.g., peptide derivatives (for example, that contain one or more non-naturally occurring amino acids) can also be used. One example of these are peptoid libraries (Simon et al., 1992, *Proc. Natl. Acad. Sci. USA* 89:9367-9371). Peptoids are polymers of non-natural amino acids that have naturally occurring side

chains attached not to the α carbon but to the backbone amino nitrogen. Since peptoids are not easily degraded by human digestive enzymes, they are advantageously more easily adaptable to drug use. Another example of a library that can be used, in which the amide functionalities in peptides have been permethylated to generate a chemically transformed combinatorial library, is described by Ostresh et al., 1994, Proc. Natl. Acad. Sci. USA 91:11138-11142).

The members of the peptide libraries that can be screened according to the invention are not limited to containing the 20 naturally occurring amino acids. In particular, chemically synthesized libraries and polysome based libraries allow the use of amino acids in addition to the 20 naturally occurring amino acids (by their inclusion in the precursor pool of amino acids used in library production). In specific embodiments, the library members contain one or more non-natural or non-classical amino acids or cyclic peptides. Non-classical amino acids include but are not limited to the D-isomers of the common amino acids, -amino isobutyric acid, 4-aminobutyric acid, Abu, 2-amino butyric acid; -Abu, -Ahx, 6-amino hexanoic acid; Aib, 2-amino isobutyric acid; 3-amino propionic acid; ornithine; norleucine; norvaline, hydroxyproline, sarcosine, citrulline, cysteic acid, t-butylglycine, t-butylalanine, phenylglycine, cyclohexylalanine, β -alanine, designer amino acids such as β -methyl amino acids, C-methyl amino acids, N-methyl amino acids, fluoro-amino acids and amino acid analogs in general. Furthermore, the amino acid can be D (dextrorotary) or L (levorotary).

In a specific embodiment, fragments and/or analogs of complexes of the invention, or protein components thereof, especially peptidomimetics, are screened for activity as competitive or non-competitive inhibitors of complex activity or formation.

In another embodiment of the present invention, combinatorial chemistry can be used to identify modulators of the complexes. Combinatorial chemistry is capable of creating libraries containing hundreds of thousands of compounds, many of which may be structurally similar. While high throughput screening programs are capable of screening these vast libraries for affinity for known targets, new approaches have been developed that achieve libraries of smaller dimension but which provide maximum chemical diversity. (See e.g., Matter, 1997, J. Med. Chem. 40:1219-1229).

One method of combinatorial chemistry, affinity fingerprinting, has previously been used to test a discrete library of small molecules for binding affinities for a defined panel of proteins. The fingerprints obtained by the screen are used to predict the affinity of the individual library members for other proteins or receptors of interest (in the instant

invention, the protein complexes of the present invention and protein components thereof.) The fingerprints are compared with fingerprints obtained from other compounds known to react with the protein of interest to predict whether the library compound might similarly react. For example, rather than testing every ligand in a large library for interaction with a complex or protein component, only those ligands having a fingerprint similar to other compounds known to have that activity could be tested. (See, e.g., Kauvar et al., 1995, *Chem. Biol.* 2:107-118; Kauvar, 1995, *Affinity fingerprinting, Pharmaceutical Manufacturing International.* 8:25-28; and Kauvar, *Toxic-Chemical Detection by Pattern Recognition in New Frontiers in Agrochemical Immunoassay*, Kurtz, Stanker and Skerritt (eds), 1995, AOAC: Washington, D.C., 305-312).

Kay et al. (1993, *Gene* 128:59-65) disclosed a method of constructing peptide libraries that encode peptides of totally random sequence that are longer than those of any prior conventional libraries. The libraries disclosed in Kay et al. encode totally synthetic random peptides of greater than about 20 amino acids in length. Such libraries can be advantageously screened to identify complex modulators. (See also U.S. Patent No. 5,498,538 dated March 12, 1996; and PCT Publication No. WO 94/18318 dated August 18, 1994).

A comprehensive review of various types of peptide libraries can be found in Gallop et al., 1994, *J. Med. Chem.* 37:1233-1251.

4.7 PHARMACEUTICAL COMPOSITIONS AND THERAPEUTIC/PROPHYLACTIC ADMINISTRATION

The invention provides methods of treatment (and prophylaxis) by administration to a subject of an effective amount of a therapeutic of the invention. In a preferred aspect, the therapeutic is substantially purified. The subject is preferably an animal including, but not limited to animals such as cows, pigs, horses, chickens, cats, dogs, etc., and is preferably a mammal, and most preferably human. In a specific embodiment, a non-human mammal is the subject.

Various delivery systems are known and can be used to administer a therapeutic of the invention, e.g., encapsulation in liposomes, microparticles, and microcapsules; use of recombinant cells capable of expressing the therapeutic, use of receptor-mediated endocytosis (e.g., Wu and Wu, 1987, *J. Biol. Chem.* 262:4429-4432); construction of a

therapeutic nucleic acid as part of a retroviral or other vector, etc. Methods of introduction include but are not limited to intradermal, intramuscular, intraperitoneal, intravenous, subcutaneous, intranasal, epidural, and oral routes. The compounds may be administered by any convenient route, for example by infusion, by bolus injection, by absorption through epithelial or mucocutaneous linings (e.g., oral, rectal and intestinal mucosa, etc.), and may be administered together with other biologically active agents. Administration can be systemic or local. In addition, it may be desirable to introduce the pharmaceutical compositions of the invention into the central nervous system by any suitable route, including intraventricular and intrathecal injection; intraventricular injection may be facilitated by an intraventricular catheter, for example, attached to a reservoir, such as an Ommaya reservoir. Pulmonary administration can also be employed, e.g., by use of an inhaler or nebulizer, and formulation with an aerosolizing agent.

In a specific embodiment, it may be desirable to administer the pharmaceutical compositions of the invention locally to the area in need of treatment. This may be achieved by, for example, and not by way of limitation, local infusion during surgery, topical application, e.g., in conjunction with a wound dressing after surgery, by injection, by means of a catheter, by means of a suppository, or by means of an implant, said implant being of a porous, non-porous, or gelatinous material, including membranes, such as sialastic membranes, or fibers. In one embodiment, administration can be by direct injection at the site (or former site) of a malignant tumor or neoplastic or pre-neoplastic tissue.

In another embodiment, the therapeutic can be delivered in a vesicle, in particular a liposome (Langer, 1990, *Science* 249:1527-1533; Treat et al., 1989, In: *Liposomes in the Therapy of Infectious Disease and Cancer*, Lopez-Berestein and Fidler, eds., Liss, New York, pp. 353-365; Lopez-Berestein, *ibid.*, pp. 317-327; see generally *ibid.*)

In yet another embodiment, the therapeutic can be delivered via a controlled release system. In one embodiment, a pump may be used (Langer, *supra*; Sefton, 1987, *CRC Crit. Ref. Biomed. Eng.* 14:201-240; Buchwald et al., 1980, *Surgery* 88:507-516; Saudek et al., 1989, *N. Engl. J. Med.* 321:574-579). In another embodiment, polymeric materials can be used (*Medical Applications of Controlled Release*, Langer and Wise, eds., CRC Press, Boca Raton, Florida, 1974; *Controlled Drug Bioavailability, Drug Product Design and Performance*, Smolen and Ball, eds., Wiley, New York, 1984; Ranger and Peppas, 1983, *Macromol. Sci. Rev. Macromol. Chem.* 23:61; Levy et al., 1985, *Science* 228:190-192; During et al., 1989, *Ann. Neurol.* 25:351-356; Howard et al.,

1989, J. Neurosurg. 71:858-863). In yet another embodiment, a controlled release system can be placed in proximity of the therapeutic target, i.e., the brain, thus requiring only a fraction of the systemic dose (e.g., Goodson, 1984, In: Medical Applications of Controlled Release, supra, Vol. 2, pp. 115-138). Other controlled release systems are discussed in the review by Langer (1990, Science 249:1527-1533).

In a specific embodiment where the therapeutic is a nucleic acid encoding a protein therapeutic, the nucleic acid can be administered *in vivo* to promote expression of its encoded protein, by constructing it as part of an appropriate nucleic acid expression vector and administering it so that it becomes intracellular, e.g., by use of a retroviral vector (U.S. Patent No. 4,980,286), or by direct injection, or by use of microparticle bombardment (e.g., a gene gun; Biolistic, Dupont), or by coating it with lipids, cell-surface receptors or transfecting agents, or by administering it in linkage to a homeobox-like peptide which is known to enter the nucleus (e.g., Joliot et al., 1991, Proc. Natl. Acad. Sci. USA 88:1864-1868), etc. Alternatively, a nucleic acid therapeutic can be introduced intracellularly and incorporated by homologous recombination within host cell DNA for expression.

The present invention also provides pharmaceutical compositions. Such compositions comprise a therapeutically effective amount of a therapeutic, and a pharmaceutically acceptable carrier. In a specific embodiment, the term "pharmaceutically acceptable" means approved by a regulatory agency of the Federal or a state government or listed in the U.S. Pharmacopeia or other generally recognized pharmacopeia for use in animals, and more particularly, in humans. The term "carrier" refers to a diluent, adjuvant, excipient, or vehicle with which the therapeutic is administered. Such pharmaceutical carriers can be sterile liquids, such as water and oils, including those of petroleum, animal, vegetable or synthetic origin, including but not limited to peanut oil, soybean oil, mineral oil, sesame oil and the like. Water is a preferred carrier when the pharmaceutical composition is administered orally. Saline and aqueous dextrose are preferred carriers when the pharmaceutical composition is administered intravenously. Saline solutions and aqueous dextrose and glycerol solutions are preferably employed as liquid carriers for injectable solutions. Suitable pharmaceutical excipients include starch, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, sodium stearate, glycerol monostearate, talc, sodium chloride, dried skim milk, glycerol, propylene, glycol, water, ethanol and the like. The composition, if desired, can also contain minor amounts of wetting or emulsifying agents, or pH

buffering agents. These compositions can take the form of solutions, suspensions, emulsions, tablets, pills, capsules, powders, sustained-release formulations and the like. The composition can be formulated as a suppository, with traditional binders and carriers such as triglycerides. Oral formulation can include standard carriers such as pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, sodium saccharine, cellulose, magnesium carbonate, etc. Examples of suitable pharmaceutical carriers are described in "Remington's Pharmaceutical Sciences" by E.W. Martin. Such compositions will contain a therapeutically effective amount of the therapeutic, preferably in purified form, together with a suitable amount of carrier so as to provide the form for proper administration to the patient. The formulation should suit the mode of administration.

In a preferred embodiment, the composition is formulated, in accordance with routine procedures, as a pharmaceutical composition adapted for intravenous administration to human beings. Typically, compositions for intravenous administration are solutions in sterile isotonic aqueous buffer. Where necessary, the composition may also include a solubilizing agent and a local anesthetic such as lidocaine to ease pain at the site of the injection. Generally, the ingredients are supplied either separately or mixed together in unit dosage form, for example, as a dry lyophilized powder or water-free concentrate in a hermetically sealed container such as an ampoule or sachette indicating the quantity of active agent. Where the composition is to be administered by infusion, it can be dispensed with an infusion bottle containing sterile pharmaceutical grade water or saline. Where the composition is administered by injection, an ampoule of sterile water or saline for injection can be provided so that the ingredients may be mixed prior to administration.

The therapeutics of the invention can be formulated as neutral or salt forms. Pharmaceutically acceptable salts include those formed with free carboxyl groups such as those derived from hydrochloric, phosphoric, acetic, oxalic, tartaric acids, etc., those formed with free amine groups such as those derived from isopropylamine, triethylamine, 2-ethylamino ethanol, histidine, procaine, etc., and those derived from sodium, potassium, ammonium, calcium, and ferric hydroxides, etc.

The amount of the therapeutic of the invention which will be effective in the treatment of a particular disorder or condition will depend on the nature of the disorder or condition, and can be determined by standard clinical techniques. In addition, in vitro assays may optionally be employed to help identify optimal dosage ranges. The precise

dose to be employed in the formulation will also depend on the route of administration, and the seriousness of the disease or disorder, and should be decided according to the judgment of the practitioner and each patient's circumstances. However, suitable dosage ranges for intravenous administration are generally about 20-500 micrograms of active compound per kilogram body weight. Suitable dosage ranges for intranasal administration are generally about 0.01 pg/kg body weight to 1 mg/kg body weight. Effective doses may be extrapolated from dose-response curves derived from in vitro or animal model test systems.

Suppositories generally contain active ingredient in the range of 0.5% to 10% by weight; oral formulations preferably contain 10% to 95% active ingredient.

The invention also provides a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the pharmaceutical compositions of the invention. Optionally associated with such container(s) can be a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration.

The invention also provides a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the pharmaceutical compositions of the invention. For example, the kit can comprise in one or more containers a first protein, or a functionally active fragment or functionally active derivative thereof, which first protein is selected from the group consisting of proteins listed in the fourth column of table 1; and a second protein, or a functionally active fragment or functionally active derivative thereof, which second protein is selected from the group consisting of proteins listed in the fifth column of table 1.

Alternatively, the kit can comprise in one or more containers, all proteins, functionally active fragments or functionally active derivatives thereof from the group of proteins in the sixth column of table 1.

The kits of the present invention can also contain expression vectors encoding the essential components of the complex machinery, which components after being expressed can be reconstituted in order to form a biologically active complex. Such a kit preferably also contains the required buffers and reagents. Optionally associated with such container(s) can be instructions for use of the kit and/or a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of

pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration.

4.8 ANIMAL MODELS

The present invention also provides animal models. In one embodiment, animal models for diseases and disorders involving the protein complexes of the present invention are provided. These animal models are well known in the art. These animal models include, but are not limited to those which are listed in the section 4.6 (supra) as exemplary animal models to study any of the complexes provided in the invention. Such animals can be initially produced by promoting homologous recombination or insertional mutagenesis between genes encoding the protein components of the complexes in the chromosome, and exogenous genes encoding the protein components of the complexes that have been rendered biologically inactive or deleted (preferably by insertion of a heterologous sequence, e.g., an antibiotic resistance gene). In a preferred aspect, homologous recombination is carried out by transforming embryo-derived stem (ES) cells with one or more vectors containing one or more insertionally inactivated genes, such that homologous recombination occurs, followed by injecting the transformed ES cells into a blastocyst, and implanting the blastocyst into a foster mother, followed by the birth of the chimeric animal ("knockout animal") in which a gene encoding a component protein from the fourth column of table 1, or a functionally active fragment or functionally active derivative thereof, and a gene encoding a component protein from the fifth column of table 1, or a functionally active fragment or functionally active derivative thereof, has been inactivated or deleted (Capecchi, 1989, Science 244:1288-1292).

In another preferred aspect, homologous recombination is carried out by transforming embryo-derived stem (ES) cells with one or more vectors containing one or more insertionally inactivated genes, such that homologous recombination occurs, followed by injecting the transformed ES cells into a blastocyst, and implanting the blastocyst into a foster mother, followed by the birth of the chimeric animal ("knockout animal") in which the genes of all component proteins from the group of proteins listed in the fourth column of table 1 or of all proteins from the group of proteins listed in the fifth column of table 1 have been inactivated or deleted.

The chimeric animal can be bred to produce additional knockout animals. Such animals can be mice, hamsters, sheep, pigs, cattle, etc., and are preferably non-human mammals. In a specific embodiment, a knockout mouse is produced.

Such knockout animals are expected to develop, or be predisposed to developing, diseases or disorders associated with mutations involving the protein complexes of the present invention, and thus, can have use as animal models of such diseases and disorders, e.g., to screen for or test molecules (e.g., potential therapeutics) for such diseases and disorders.

In a different embodiment of the invention, transgenic animals that have incorporated and express (or over-express or mis-express) a functional gene encoding a protein component of the complex, e.g. by introducing the a gene encoding one or more of the components of the complex under the control of a heterologous promoter (i.e., a promoter that is not the native promoter of the gene) that either over-expresses the protein or proteins, or expresses them in tissues not normally expressing the complexes or proteins, can have use as animal models of diseases and disorders characterized by elevated levels of the protein complexes. Such animals can be used to screen or test molecules for the ability to treat or prevent the diseases and disorders cited supra.

In one embodiment, the present invention provides a recombinant non-human animal in which an endogenous gene encoding a first protein, or a functionally active fragment or functionally active derivative thereof, which first protein is selected from the group of proteins listed in the fourth column of table 1, and and endogenous gene encoding a second protein, or a functionally active fragment or functionally active derivative thereof, which second protein is selected from the group consisting of proteins listed in the fifth column of table 1 has been deleted or inactivated by homologous recombination or insertional mutagenesis of said animal or an ancestor thereof. In addition, the present invention provides a recombinant non-human animal in which the endogenous genes of all proteins, or functionally active fragments or functionally active derivatives thereof of one of the group of proteins listed in the sixth column have been deleted or inactivated by homologous recombination or insertional mutagenesis of said animal or an ancestor thereof:

In another embodiment, the present invention provides a recombinant non-human animal in which an endogenous gene encoding a first protein, or a functionally active fragment or functionally active derivative thereof, which first protein is selected from the group consisting of proteins of the fourth column of table 1, and endogenous gene

encoding a second protein, or a functionally active fragment or functionally active derivative thereof, which second protein is selected from the group consisting of proteins of the fifth column, of table 1 are recombinantly expressed in said animal or an ancestor thereof.

The following series of examples are presented by way of illustration and not by way of limitation on the scope of the invention.

EXAMPLES

An object of the present invention was to identify protein complexes of the APP processing pathway, component proteins of the said complexes, fragments and derivatives of the component proteins, and antibodies specific to the complexes. The present invention also relates to methods for use of the complexes of the APP processing pathway and their interacting proteins in, inter alia, screening, diagnosis, and therapy, as well as to methods of preparing the complexes.

By applying the process according to the invention said complexes were identified. The components are listed in table 1.

APP-C59-complex, Bace1-complex, Bace2-complex, BRI-complex, mDab1-complex, Fe65L2-complex, Plit-complex, Paladin-complex, Neurotrypsin-complex, Hunc18a-complex, Telencephalin-complex, PC7-complex, TFCP2-complex, Jip1-complex, Lamezin-complex, VTRP-complex, p75-NTR-complex

Said object is further achieved by the characterization of component proteins. These proteins are listed in table 2.

Thus, the invention relates to the following embodiments:

The invention relates to the following embodiments of the mDab1-complex

1. A protein complex selected from complex (I) and comprising
 - (a) at least one first protein selected from the group consisting of:
 - (i) "APLP1" (SEQ ID No:3) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a

nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,

(ii) "APLP2" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,

(iii) "APP" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,

(iv) "ApoE receptor 2" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ApoE receptor 2" encoded by a nucleic acid that hybridizes to the "ApoE receptor 2" nucleic acid or its complement under low stringency conditions,

(v) "DAB1" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAB1" encoded by a nucleic acid that hybridizes to the "DAB1" nucleic acid or its complement under low stringency conditions, and

(vi) "VLDL receptor" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VLDL receptor" encoded by a nucleic acid that hybridizes to the "VLDL receptor" nucleic acid or its complement under low stringency conditions, and

(b) at least one second protein, which second protein is selected from the group consisting of:

(i) "ACE" (SEQ ID No:1) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ACE" encoded by a nucleic acid that hybridizes to the "ACE" nucleic acid or its complement under low stringency conditions,

(ii) "APG-1" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APG-1" encoded by a nucleic acid that hybridizes to the "APG-1" nucleic acid or its complement under low stringency conditions,

(iii) "Archvillin" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Archvillin" encoded by a

nucleic acid that hybridizes to the "Archvillin" nucleic acid or its complement under low stringency conditions,

(iv) "CRK" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CRK" encoded by a nucleic acid that hybridizes to the "CRK" nucleic acid or its complement under low stringency conditions,

(v) "CRKL" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CRKL" encoded by a nucleic acid that hybridizes to the "CRKL" nucleic acid or its complement under low stringency conditions,

(vi) "CSNK1D" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CSNK1D" encoded by a nucleic acid that hybridizes to the "CSNK1D" nucleic acid or its complement under low stringency conditions,

(vii) "CSNK1E" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CSNK1E" encoded by a nucleic acid that hybridizes to the "CSNK1E" nucleic acid or its complement under low stringency conditions,

(viii) "Contactin1" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Contactin1" encoded by a nucleic acid that hybridizes to the "Contactin1" nucleic acid or its complement under low stringency conditions,

(ix) "DAB2IP" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAB2IP" encoded by a nucleic acid that hybridizes to the "DAB2IP" nucleic acid or its complement under low stringency conditions,

(x) "DNAJB1" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNAJB1" encoded by a nucleic acid that hybridizes to the "DNAJB1" nucleic acid or its complement under low stringency conditions,

(xi) "Hypothetical protein FLJ31432" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ31432" encoded by a nucleic acid that hybridizes to the

"Hypothetical protein FLJ31432" nucleic acid or its complement under low stringency conditions,

(xii) "ISL1" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ISL1" encoded by a nucleic acid that hybridizes to the "ISL1" nucleic acid or its complement under low stringency conditions,

(xiii) "ITGA1" (SEQ ID No:18) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITGA1" encoded by a nucleic acid that hybridizes to the "ITGA1" nucleic acid or its complement under low stringency conditions,

(xiv) "ITGB1" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITGB1" encoded by a nucleic acid that hybridizes to the "ITGB1" nucleic acid or its complement under low stringency conditions,

(xv) "LDLR" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LDLR" encoded by a nucleic acid that hybridizes to the "LDLR" nucleic acid or its complement under low stringency conditions,

(xvi) "MAPK8IP3/JIP3" (SEQ ID No:21) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MAPK8IP3/JIP3" encoded by a nucleic acid that hybridizes to the "MAPK8IP3/JIP3" nucleic acid or its complement under low stringency conditions,

(xvii) "NEDD5" (SEQ ID No:22) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEDD5" encoded by a nucleic acid that hybridizes to the "NEDD5" nucleic acid or its complement under low stringency conditions,

(xviii) "PLK" (SEQ ID No:23) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PLK" encoded by a nucleic acid that hybridizes to the "PLK" nucleic acid or its complement under low stringency conditions,

(xix) "Proto-oncogene tyrosine kinase FYN (P59-FYN, SYN, SLK) isoform 1" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Proto-oncogene tyrosine kinase FYN (P59-FYN, SYN, SLK) isoform 1" encoded by a nucleic acid that hybridizes to the "Proto-

oncogene tyrosine kinase FYN (P59-FYN, SYN, SLK) isoform 1" nucleic acid or its complement under low stringency conditions,

(xx) "QPRT" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "QPRT" encoded by a nucleic acid that hybridizes to the "QPRT" nucleic acid or its complement under low stringency conditions,

(xxi) "S-100 beta" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions,

(xxii) "SIM TO PLEXIN 1 - MOUSE" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIM TO PLEXIN 1 - MOUSE" encoded by a nucleic acid that hybridizes to the "SIM TO PLEXIN 1 - MOUSE" nucleic acid or its complement under low stringency conditions,

(xxiii) "TGM5" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TGM5" encoded by a nucleic acid that hybridizes to the "TGM5" nucleic acid or its complement under low stringency conditions, and

(xxiv) "hypothetical protein FLJ11151" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein FLJ11151" encoded by a nucleic acid that hybridizes to the "hypothetical protein FLJ11151" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

2. The protein complex according to No. 1 wherein the first protein is the protein Dab1 (SEQ ID NO. 13), or a functionally active derivative thereof, or a functionally active

fragment thereof, or a homolog thereof, or a variant of 'Dab1' encoded by a nucleic acid that hybridizes to the 'Dab1' under low stringency conditions.

3. The protein complex according to No. 1 selected from complex (I) and comprising the following proteins:

- (i) "ACE" (SEQ ID No:1) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ACE" encoded by a nucleic acid that hybridizes to the "ACE" nucleic acid or its complement under low stringency conditions,
- (ii) "APG-1" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APG-1" encoded by a nucleic acid that hybridizes to the "APG-1" nucleic acid or its complement under low stringency conditions,
- (iii) "APLP1" (SEQ ID No:3) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,
- (iv) "APLP2" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,
- (v) "APP" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (vi) "ApoE receptor 2" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ApoE receptor 2" encoded by a nucleic acid that hybridizes to the "ApoE receptor 2" nucleic acid or its complement under low stringency conditions,
- (vii) "Archvillin" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Archvillin" encoded by a nucleic acid that hybridizes to the "Archvillin" nucleic acid or its complement under low stringency conditions,

- (viii) "CRK" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CRK" encoded by a nucleic acid that hybridizes to the "CRK" nucleic acid or its complement under low stringency conditions,
- (ix) "CRKL" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CRKL" encoded by a nucleic acid that hybridizes to the "CRKL" nucleic acid or its complement under low stringency conditions,
- (x) "CSNK1D" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CSNK1D" encoded by a nucleic acid that hybridizes to the "CSNK1D" nucleic acid or its complement under low stringency conditions,
- (xi) "CSNK1E" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CSNK1E" encoded by a nucleic acid that hybridizes to the "CSNK1E" nucleic acid or its complement under low stringency conditions,
- (xii) "Contactin1" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Contactin1" encoded by a nucleic acid that hybridizes to the "Contactin1" nucleic acid or its complement under low stringency conditions,
- (xiii) "DAB1" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAB1" encoded by a nucleic acid that hybridizes to the "DAB1" nucleic acid or its complement under low stringency conditions,
- (xiv) "DAB2IP" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAB2IP" encoded by a nucleic acid that hybridizes to the "DAB2IP" nucleic acid or its complement under low stringency conditions,
- (xv) "DNAJB1" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNAJB1" encoded by a nucleic acid that hybridizes to the "DNAJB1" nucleic acid or its complement under low stringency conditions,
- (xvi) "Hypothetical protein FLJ31432" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"Hypothetical protein FLJ31432" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ31432" nucleic acid or its complement under low stringency conditions,

(xvii) "ISL1" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ISL1" encoded by a nucleic acid that hybridizes to the "ISL1" nucleic acid or its complement under low stringency conditions,

(xviii) "ITGA1" (SEQ ID No:18) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITGA1" encoded by a nucleic acid that hybridizes to the "ITGA1" nucleic acid or its complement under low stringency conditions,

(xix) "ITGB1" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITGB1" encoded by a nucleic acid that hybridizes to the "ITGB1" nucleic acid or its complement under low stringency conditions,

(xx) "LDLR" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LDLR" encoded by a nucleic acid that hybridizes to the "LDLR" nucleic acid or its complement under low stringency conditions,

(xxi) "MAPK8IP3/JIP3" (SEQ ID No:21) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MAPK8IP3/JIP3" encoded by a nucleic acid that hybridizes to the "MAPK8IP3/JIP3" nucleic acid or its complement under low stringency conditions,

(xxii) "NEDD5" (SEQ ID No:22) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEDD5" encoded by a nucleic acid that hybridizes to the "NEDD5" nucleic acid or its complement under low stringency conditions,

(xxiii) "PLK" (SEQ ID No:23) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PLK" encoded by a nucleic acid that hybridizes to the "PLK" nucleic acid or its complement under low stringency conditions,

(xxiv) "Proto-oncogene tyrosine kinase FYN (P59-FYN, SYN, SLK) isoform 1" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Proto-oncogene tyrosine kinase FYN (P59-

FYN, SYN, SLK) isoform 1" encoded by a nucleic acid that hybridizes to the "Proto-oncogene tyrosine kinase FYN (P59-FYN, SYN, SLK) isoform 1" nucleic acid or its complement under low stringency conditions,

(xxv) "QPRT" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "QPRT" encoded by a nucleic acid that hybridizes to the "QPRT" nucleic acid or its complement under low stringency conditions,

(xxvi) "S-100 beta" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions,

(xxvii) "SIM TO PLEXIN 1 - MOUSE" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIM TO PLEXIN 1 - MOUSE" encoded by a nucleic acid that hybridizes to the "SIM TO PLEXIN 1 - MOUSE" nucleic acid or its complement under low stringency conditions,

(xxviii) "TGM5" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TGM5" encoded by a nucleic acid that hybridizes to the "TGM5" nucleic acid or its complement under low stringency conditions,

(xxix) "VLDL receptor" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VLDL receptor" encoded by a nucleic acid that hybridizes to the "VLDL receptor" nucleic acid or its complement under low stringency conditions, and/or

(xxx) "hypothetical protein FLJ11151" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein FLJ11151" encoded by a nucleic acid that hybridizes to the "hypothetical protein FLJ11151" nucleic acid or its complement under low stringency conditions,

and a protein complex selected from complex (II) and comprising the following proteins:

(i) "ACE" (SEQ ID No:1) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ACE" encoded by a nucleic acid that hybridizes to the "ACE" nucleic acid or its complement under low stringency conditions,

- (ii) "APG-1" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APG-1" encoded by a nucleic acid that hybridizes to the "APG-1" nucleic acid or its complement under low stringency conditions,
- (iii) "APLP1" (SEQ ID No:3) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,
- (iv) "APLP2" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,
- (v) "APP" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (vi) "Archvillin" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Archvillin" encoded by a nucleic acid that hybridizes to the "Archvillin" nucleic acid or its complement under low stringency conditions,
- (vii) "CRK" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CRK" encoded by a nucleic acid that hybridizes to the "CRK" nucleic acid or its complement under low stringency conditions,
- (viii) "CRKL" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CRKL" encoded by a nucleic acid that hybridizes to the "CRKL" nucleic acid or its complement under low stringency conditions,
- (ix) "CSNK1D" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CSNK1D" encoded by a nucleic acid that hybridizes to the "CSNK1D" nucleic acid or its complement under low stringency conditions,
- (x) "CSNK1E" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CSNK1E" encoded by a

nucleic acid that hybridizes to the "CSNK1E" nucleic acid or its complement under low stringency conditions,

(xi) "Contactin1" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Contactin1" encoded by a nucleic acid that hybridizes to the "Contactin1" nucleic acid or its complement under low stringency conditions,

(xii) "DAB1" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAB1" encoded by a nucleic acid that hybridizes to the "DAB1" nucleic acid or its complement under low stringency conditions,

(xiii) "DAB2IP" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAB2IP" encoded by a nucleic acid that hybridizes to the "DAB2IP" nucleic acid or its complement under low stringency conditions,

(xiv) "DNAJB1" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNAJB1" encoded by a nucleic acid that hybridizes to the "DNAJB1" nucleic acid or its complement under low stringency conditions,

(xv) "Hypothetical protein FLJ31432" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ31432" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ31432" nucleic acid or its complement under low stringency conditions,

(xvi) "ISL1" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ISL1" encoded by a nucleic acid that hybridizes to the "ISL1" nucleic acid or its complement under low stringency conditions,

(xvii) "ITGA1" (SEQ ID No:18) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITGA1" encoded by a nucleic acid that hybridizes to the "ITGA1" nucleic acid or its complement under low stringency conditions,

(xviii) "ITGB1" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITGB1" encoded by a

nucleic acid that hybridizes to the "ITGB1" nucleic acid or its complement under low stringency conditions,

(xix) "LDLR" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LDLR" encoded by a nucleic acid that hybridizes to the "LDLR" nucleic acid or its complement under low stringency conditions,

(xx) "MAPK8IP3/JIP3" (SEQ ID No:21) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MAPK8IP3/JIP3" encoded by a nucleic acid that hybridizes to the "MAPK8IP3/JIP3" nucleic acid or its complement under low stringency conditions,

(xxi) "NEDD5" (SEQ ID No:22) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEDD5" encoded by a nucleic acid that hybridizes to the "NEDD5" nucleic acid or its complement under low stringency conditions,

(xxii) "PLK" (SEQ ID No:23) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PLK" encoded by a nucleic acid that hybridizes to the "PLK" nucleic acid or its complement under low stringency conditions,

(xxiii) "Proto-oncogene tyrosine kinase FYN (P59-FYN, SYN, SLK) isoform 1" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Proto-oncogene tyrosine kinase FYN (P59-FYN, SYN, SLK) isoform 1" encoded by a nucleic acid that hybridizes to the "Proto-oncogene tyrosine kinase FYN (P59-FYN, SYN, SLK) isoform 1" nucleic acid or its complement under low stringency conditions,

(xxiv) "QPRT" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "QPRT" encoded by a nucleic acid that hybridizes to the "QPRT" nucleic acid or its complement under low stringency conditions,

(xxv) "S-100 beta" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions,

(xxvi) "SIM TO PLEXIN 1 - MOUSE" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"SIM TO PLEXIN 1 - MOUSE" encoded by a nucleic acid that hybridizes to the "SIM TO PLEXIN 1 - MOUSE" nucleic acid or its complement under low stringency conditions,

(xxvii) "TGM5" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TGM5" encoded by a nucleic acid that hybridizes to the "TGM5" nucleic acid or its complement under low stringency conditions, and/or

(xxviii) "hypothetical protein FLJ11151" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein FLJ11151" encoded by a nucleic acid that hybridizes to the "hypothetical protein FLJ11151" nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 23 of the following proteins:

- (i) "ACE" (SEQ ID No:1) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ACE" encoded by a nucleic acid that hybridizes to the "ACE" nucleic acid or its complement under low stringency conditions,
- (ii) "APG-1" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APG-1" encoded by a nucleic acid that hybridizes to the "APG-1" nucleic acid or its complement under low stringency conditions,
- (iii) "APLP1" (SEQ ID No:3) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,
- (iv) "APLP2" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,
- (v) "APP" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,

- (vi) "ApoE receptor 2" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ApoE receptor 2" encoded by a nucleic acid that hybridizes to the "ApoE receptor 2" nucleic acid or its complement under low stringency conditions,
- (vii) "Archvillin" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Archvillin" encoded by a nucleic acid that hybridizes to the "Archvillin" nucleic acid or its complement under low stringency conditions,
- (viii) "CRK" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CRK" encoded by a nucleic acid that hybridizes to the "CRK" nucleic acid or its complement under low stringency conditions,
- (ix) "CRKL" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CRKL" encoded by a nucleic acid that hybridizes to the "CRKL" nucleic acid or its complement under low stringency conditions,
- (x) "CSNK1D" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CSNK1D" encoded by a nucleic acid that hybridizes to the "CSNK1D" nucleic acid or its complement under low stringency conditions,
- (xi) "CSNK1E" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CSNK1E" encoded by a nucleic acid that hybridizes to the "CSNK1E" nucleic acid or its complement under low stringency conditions,
- (xii) "Contactin1" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Contactin1" encoded by a nucleic acid that hybridizes to the "Contactin1" nucleic acid or its complement under low stringency conditions,
- (xiii) "DAB1" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAB1" encoded by a nucleic acid that hybridizes to the "DAB1" nucleic acid or its complement under low stringency conditions,
- (xiv) "DAB2IP" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAB2IP" encoded by a

nucleic acid that hybridizes to the "DAB2IP" nucleic acid or its complement under low stringency conditions,

(xv) "DNAJB1" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNAJB1" encoded by a nucleic acid that hybridizes to the "DNAJB1" nucleic acid or its complement under low stringency conditions,

(xvi) "Hypothetical protein FLJ31432" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ31432" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ31432" nucleic acid or its complement under low stringency conditions,

(xvii) "ISL1" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ISL1" encoded by a nucleic acid that hybridizes to the "ISL1" nucleic acid or its complement under low stringency conditions,

(xviii) "ITGA1" (SEQ ID No:18) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITGA1" encoded by a nucleic acid that hybridizes to the "ITGA1" nucleic acid or its complement under low stringency conditions,

(xix) "ITGB1" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITGB1" encoded by a nucleic acid that hybridizes to the "ITGB1" nucleic acid or its complement under low stringency conditions,

(xx) "LDLR" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LDLR" encoded by a nucleic acid that hybridizes to the "LDLR" nucleic acid or its complement under low stringency conditions,

(xxi) "MAPK8IP3/JIP3" (SEQ ID No:21) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MAPK8IP3/JIP3" encoded by a nucleic acid that hybridizes to the "MAPK8IP3/JIP3" nucleic acid or its complement under low stringency conditions,

(xxii) "NEDD5" (SEQ ID No:22) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEDD5"

- encoded by a nucleic acid that hybridizes to the "NEDD5" nucleic acid or its complement under low stringency conditions,
- (xxiii) "PLK" (SEQ ID No:23) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PLK" encoded by a nucleic acid that hybridizes to the "PLK" nucleic acid or its complement under low stringency conditions,
- (xxiv) "Proto-oncogene tyrosine kinase FYN (P59-FYN, SYN, SLK) isoform 1" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Proto-oncogene tyrosine kinase FYN (P59-FYN, SYN, SLK) isoform 1" encoded by a nucleic acid that hybridizes to the "Proto-oncogene tyrosine kinase FYN (P59-FYN, SYN, SLK) isoform 1" nucleic acid or its complement under low stringency conditions,
- (xxv) "QPRT" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "QPRT" encoded by a nucleic acid that hybridizes to the "QPRT" nucleic acid or its complement under low stringency conditions,
- (xxvi) "S-100 beta" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions,
- (xxvii) "SIM TO PLEXIN 1 - MOUSE" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIM TO PLEXIN 1 - MOUSE" encoded by a nucleic acid that hybridizes to the "SIM TO PLEXIN 1 - MOUSE" nucleic acid or its complement under low stringency conditions,
- (xxviii) "TGM5" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TGM5" encoded by a nucleic acid that hybridizes to the "TGM5" nucleic acid or its complement under low stringency conditions,
- (xxix) "VLDL receptor" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VLDL receptor" encoded by a nucleic acid that hybridizes to the "VLDL receptor" nucleic acid or its complement under low stringency conditions,
- (xxx) "hypothetical protein FLJ11151" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"hypothetical protein FLJ11151" encoded by a nucleic acid that hybridizes to the "hypothetical protein FLJ11151" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.
6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.
7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.
8. The complex of any of No. 1 - 7 that is involved in the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).
9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps: expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is

attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.

10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.

11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.

12. Component of the Dab1 complex obtainable by a process according to any of No. 9 - 11.

13. Protein of the Dab1 complex selected from

(i) "DNAJB1" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNAJB1" encoded by a nucleic acid that hybridizes to the "DNAJB1" nucleic acid or its complement under low stringency conditions,

(ii) "Hypothetical protein FLJ31432" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ31432" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ31432" nucleic acid or its complement under low stringency conditions, and

(iii) "hypothetical protein FLJ11151" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein FLJ11151" encoded by a nucleic acid that hybridizes to the "hypothetical protein FLJ11151" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

14. Nucleic acid encoding a protein according to No. 13.
15. Construct, preferably a vector construct, comprising (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or
(b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).
16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).
17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.
18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.
19. The kit according to No. 18 for processing a substrate of said complex.

20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative disease such as Alzheimer's disease;.

21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.

22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.

23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:

(i) "DNAJB1" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNAJB1" encoded by a nucleic acid that hybridizes to the "DNAJB1" nucleic acid or its complement under low stringency conditions,

(ii) "Hypothetical protein FLJ31432" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ31432" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ31432" nucleic acid or its complement under low stringency conditions, and/or

(iii) "hypothetical protein FLJ11151" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein FLJ11151" encoded by a nucleic acid that hybridizes to the "hypothetical protein FLJ11151" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative disease such as Alzheimer's disease;.

25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:

- (i) "DNAJB1" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNAJB1" encoded by a nucleic acid that hybridizes to the "DNAJB1" nucleic acid or its complement under low stringency conditions,
- (ii) "Hypothetical protein FLJ31432" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ31432" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ31432" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "hypothetical protein FLJ11151" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein FLJ11151" encoded by a nucleic acid that hybridizes to the "hypothetical protein FLJ11151" nucleic acid or its complement under low stringency conditions, comprising the steps of
 - (a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and
 - (b) determinig whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of (a) exposing said complex, or a cell or organism containing Dab1 complex to one or more candidate molecules; and

- (b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a

protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.

28. The method of No. 26, wherein the activity of said complex is determined.

29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.

30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.

31. The method of No. 30, wherein said determining step comprises determining whether

(i) "ACE" (SEQ ID No:1) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ACE" encoded by a nucleic acid that hybridizes to the "ACE" nucleic acid or its complement under low stringency conditions, and/or

(ii) "APG-1" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APG-1" encoded by a nucleic acid that hybridizes to the "APG-1" nucleic acid or its complement under low stringency conditions, and/or

(iii) "APLP1" (SEQ ID No:3) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions, and/or

(iv) "APLP2" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions, and/or

- (v) "APP" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "ApoE receptor 2" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ApoE receptor 2" encoded by a nucleic acid that hybridizes to the "ApoE receptor 2" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "Archvillin" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Archvillin" encoded by a nucleic acid that hybridizes to the "Archvillin" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "CRK" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CRK" encoded by a nucleic acid that hybridizes to the "CRK" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "CRKL" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CRKL" encoded by a nucleic acid that hybridizes to the "CRKL" nucleic acid or its complement under low stringency conditions, and/or
- (x) "CSNK1D" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CSNK1D" encoded by a nucleic acid that hybridizes to the "CSNK1D" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "CSNK1E" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CSNK1E" encoded by a nucleic acid that hybridizes to the "CSNK1E" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "Contactin1" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Contactin1" encoded by a nucleic acid that hybridizes to the "Contactin1" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "DAB1" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAB1" encoded by a

nucleic acid that hybridizes to the "DAB1" nucleic acid or its complement under low stringency conditions, and/or

(xiv) "DAB2IP" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAB2IP" encoded by a nucleic acid that hybridizes to the "DAB2IP" nucleic acid or its complement under low stringency conditions, and/or

(xv) "DNAJB1" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNAJB1" encoded by a nucleic acid that hybridizes to the "DNAJB1" nucleic acid or its complement under low stringency conditions, and/or

(xvi) "Hypothetical protein FLJ31432" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ31432" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ31432" nucleic acid or its complement under low stringency conditions, and/or

(xvii) "ISL1" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ISL1" encoded by a nucleic acid that hybridizes to the "ISL1" nucleic acid or its complement under low stringency conditions, and/or

(xviii) "ITGA1" (SEQ ID No:18) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITGA1" encoded by a nucleic acid that hybridizes to the "ITGA1" nucleic acid or its complement under low stringency conditions, and/or

(xix) "ITGB1" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITGB1" encoded by a nucleic acid that hybridizes to the "ITGB1" nucleic acid or its complement under low stringency conditions, and/or

(xx) "LDLR" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LDLR" encoded by a nucleic acid that hybridizes to the "LDLR" nucleic acid or its complement under low stringency conditions, and/or

(xxi) "MAPK8IP3/JIP3" (SEQ ID No:21) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"MAPK8IP3/JIP3" encoded by a nucleic acid that hybridizes to the "MAPK8IP3/JIP3" nucleic acid or its complement under low stringency conditions, and/or

(xxii) "NEDD5" (SEQ ID No:22) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEDD5" encoded by a nucleic acid that hybridizes to the "NEDD5" nucleic acid or its complement under low stringency conditions, and/or

(xxiii) "PLK" (SEQ ID No:23) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PLK" encoded by a nucleic acid that hybridizes to the "PLK" nucleic acid or its complement under low stringency conditions, and/or

(xxiv) "Proto-oncogene tyrosine kinase FYN (P59-FYN, SYN, SLK) isoform 1" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Proto-oncogene tyrosine kinase FYN (P59-FYN, SYN, SLK) isoform 1" encoded by a nucleic acid that hybridizes to the "Proto-oncogene tyrosine kinase FYN (P59-FYN, SYN, SLK) isoform 1" nucleic acid or its complement under low stringency conditions, and/or

(xxv) "QPRT" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "QPRT" encoded by a nucleic acid that hybridizes to the "QPRT" nucleic acid or its complement under low stringency conditions, and/or

(xxvi) "S-100 beta" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and/or

(xxvii) "SIM TO PLEXIN 1 - MOUSE" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIM TO PLEXIN 1 - MOUSE" encoded by a nucleic acid that hybridizes to the "SIM TO PLEXIN 1 - MOUSE" nucleic acid or its complement under low stringency conditions, and/or

(xxviii) "TGM5" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TGM5" encoded by a nucleic acid that hybridizes to the "TGM5" nucleic acid or its complement under low stringency conditions, and/or

(xxix) "VLDL receptor" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VLDL receptor" encoded by a nucleic acid that hybridizes to the "VLDL receptor" nucleic acid or its complement under low stringency conditions, and/or
(xxx) "hypothetical protein FLJ11151" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein FLJ11151" encoded by a nucleic acid that hybridizes to the "hypothetical protein FLJ11151" nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease;.

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease;.

34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not

having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.

37. The method of No. 35, wherein the activity of said complex is determined.

38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

40. The method of No. 39, wherein said determining step comprises determining whether

(i) "ACE" (SEQ ID No:1) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ACE" encoded by a nucleic acid that hybridizes to the "ACE" nucleic acid or its complement under low stringency conditions, and/or

(ii) "APG-1" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APG-1" encoded by a nucleic acid that hybridizes to the "APG-1" nucleic acid or its complement under low stringency conditions, and/or

(iii) "APLP1" (SEQ ID No:3) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions, and/or

(iv) "APLP2" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions, and/or

- (v) "APP" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "ApoE receptor 2" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ApoE receptor 2" encoded by a nucleic acid that hybridizes to the "ApoE receptor 2" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "Archvillin" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Archvillin" encoded by a nucleic acid that hybridizes to the "Archvillin" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "CRK" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CRK" encoded by a nucleic acid that hybridizes to the "CRK" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "CRKL" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CRKL" encoded by a nucleic acid that hybridizes to the "CRKL" nucleic acid or its complement under low stringency conditions, and/or
- (x) "CSNK1D" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CSNK1D" encoded by a nucleic acid that hybridizes to the "CSNK1D" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "CSNK1E" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CSNK1E" encoded by a nucleic acid that hybridizes to the "CSNK1E" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "Contactin1" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Contactin1" encoded by a nucleic acid that hybridizes to the "Contactin1" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "DAB1" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAB1" encoded by a

nucleic acid that hybridizes to the "DAB1" nucleic acid or its complement under low stringency conditions, and/or

(xiv) "DAB2IP" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAB2IP" encoded by a nucleic acid that hybridizes to the "DAB2IP" nucleic acid or its complement under low stringency conditions, and/or

(xv) "DNAJB1" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNAJB1" encoded by a nucleic acid that hybridizes to the "DNAJB1" nucleic acid or its complement under low stringency conditions, and/or

(xvi) "Hypothetical protein FLJ31432" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ31432" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ31432" nucleic acid or its complement under low stringency conditions, and/or

(xvii) "ISL1" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ISL1" encoded by a nucleic acid that hybridizes to the "ISL1" nucleic acid or its complement under low stringency conditions, and/or

(xviii) "ITGA1" (SEQ ID No:18) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITGA1" encoded by a nucleic acid that hybridizes to the "ITGA1" nucleic acid or its complement under low stringency conditions, and/or

(xix) "ITGB1" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITGB1" encoded by a nucleic acid that hybridizes to the "ITGB1" nucleic acid or its complement under low stringency conditions, and/or

(xx) "LDLR" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LDLR" encoded by a nucleic acid that hybridizes to the "LDLR" nucleic acid or its complement under low stringency conditions, and/or

(xxi) "MAPK8IP3/JIP3" (SEQ ID No:21) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"MAPK8IP3/JIP3" encoded by a nucleic acid that hybridizes to the "MAPK8IP3/JIP3" nucleic acid or its complement under low stringency conditions, and/or

(xxii) "NEDD5" (SEQ ID No:22) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEDD5" encoded by a nucleic acid that hybridizes to the "NEDD5" nucleic acid or its complement under low stringency conditions, and/or

(xxiii) "PLK" (SEQ ID No:23) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PLK" encoded by a nucleic acid that hybridizes to the "PLK" nucleic acid or its complement under low stringency conditions, and/or

(xxiv) "Proto-oncogene tyrosine kinase FYN (P59-FYN, SYN, SLK) isoform 1" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Proto-oncogene tyrosine kinase FYN (P59-FYN, SYN, SLK) isoform 1" encoded by a nucleic acid that hybridizes to the "Proto-oncogene tyrosine kinase FYN (P59-FYN, SYN, SLK) isoform 1" nucleic acid or its complement under low stringency conditions, and/or

(xxv) "QPRT" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "QPRT" encoded by a nucleic acid that hybridizes to the "QPRT" nucleic acid or its complement under low stringency conditions, and/or

(xxvi) "S-100 beta" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and/or

(xxvii) "SIM TO PLEXIN 1 - MOUSE" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIM TO PLEXIN 1 - MOUSE" encoded by a nucleic acid that hybridizes to the "SIM TO PLEXIN 1 - MOUSE" nucleic acid or its complement under low stringency conditions, and/or

(xxviii) "TGM5" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TGM5" encoded by a nucleic acid that hybridizes to the "TGM5" nucleic acid or its complement under low stringency conditions, and/or

(xxix) "VLDL receptor" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VLDL receptor" encoded by a nucleic acid that hybridizes to the "VLDL receptor" nucleic acid or its complement under low stringency conditions, and/or
(xxx) "hypothetical protein FLJ11151" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein FLJ11151" encoded by a nucleic acid that hybridizes to the "hypothetical protein FLJ11151" nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative disease such as Alzheimer's disease;.

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42 , wherein said disease or disorder involves increased levels of the amount or activity of said complex.

45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins

- (i) "ACE" (SEQ ID No:1) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ACE" encoded by a nucleic acid that hybridizes to the "ACE" nucleic acid or its complement under low stringency conditions,
- (ii) "APG-1" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APG-1" encoded by a nucleic acid that hybridizes to the "APG-1" nucleic acid or its complement under low stringency conditions,
- (iii) "APLP1" (SEQ ID No:3) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,
- (iv) "APLP2" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,
- (v) "APP" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (vi) "ApoE receptor 2" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ApoE receptor 2" encoded by a nucleic acid that hybridizes to the "ApoE receptor 2" nucleic acid or its complement under low stringency conditions,
- (vii) "Archvillin" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Archvillin" encoded by a nucleic acid that hybridizes to the "Archvillin" nucleic acid or its complement under low stringency conditions,

- (viii) "CRK" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CRK" encoded by a nucleic acid that hybridizes to the "CRK" nucleic acid or its complement under low stringency conditions,
- (ix) "CRKL" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CRKL" encoded by a nucleic acid that hybridizes to the "CRKL" nucleic acid or its complement under low stringency conditions,
- (x) "CSNK1D" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CSNK1D" encoded by a nucleic acid that hybridizes to the "CSNK1D" nucleic acid or its complement under low stringency conditions,
- (xi) "CSNK1E" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CSNK1E" encoded by a nucleic acid that hybridizes to the "CSNK1E" nucleic acid or its complement under low stringency conditions,
- (xii) "Contactin1" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Contactin1" encoded by a nucleic acid that hybridizes to the "Contactin1" nucleic acid or its complement under low stringency conditions,
- (xiii) "DAB1" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAB1" encoded by a nucleic acid that hybridizes to the "DAB1" nucleic acid or its complement under low stringency conditions,
- (xiv) "DAB2IP" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAB2IP" encoded by a nucleic acid that hybridizes to the "DAB2IP" nucleic acid or its complement under low stringency conditions,
- (xv) "DNAJB1" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNAJB1" encoded by a nucleic acid that hybridizes to the "DNAJB1" nucleic acid or its complement under low stringency conditions,
- (xvi) "Hypothetical protein FLJ31432" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"Hypothetical protein FLJ31432" encoded by a nucleic acid that hybridizes to the

"Hypothetical protein FLJ31432" nucleic acid or its complement under low stringency conditions,

(xvii) "ISL1" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ISL1" encoded by a nucleic acid that hybridizes to the "ISL1" nucleic acid or its complement under low stringency conditions,

(xviii) "ITGA1" (SEQ ID No:18) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITGA1" encoded by a nucleic acid that hybridizes to the "ITGA1" nucleic acid or its complement under low stringency conditions,

(xix) "ITGB1" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITGB1" encoded by a nucleic acid that hybridizes to the "ITGB1" nucleic acid or its complement under low stringency conditions,

(xx) "LDLR" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LDLR" encoded by a nucleic acid that hybridizes to the "LDLR" nucleic acid or its complement under low stringency conditions,

(xxi) "MAPK8IP3/JIP3" (SEQ ID No:21) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MAPK8IP3/JIP3" encoded by a nucleic acid that hybridizes to the "MAPK8IP3/JIP3" nucleic acid or its complement under low stringency conditions,

(xxii) "NEDD5" (SEQ ID No:22) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEDD5" encoded by a nucleic acid that hybridizes to the "NEDD5" nucleic acid or its complement under low stringency conditions,

(xxiii) "PLK" (SEQ ID No:23) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PLK" encoded by a nucleic acid that hybridizes to the "PLK" nucleic acid or its complement under low stringency conditions,

(xxiv) "Proto-oncogene tyrosine kinase FYN (P59-FYN, SYN, SLK) isoform 1" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Proto-oncogene tyrosine kinase FYN (P59-

FYN, SYN, SLK) isoform 1" encoded by a nucleic acid that hybridizes to the "Proto-oncogene tyrosine kinase FYN (P59-FYN, SYN, SLK) isoform 1" nucleic acid or its complement under low stringency conditions,

(xxv) "QPRT" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "QPRT" encoded by a nucleic acid that hybridizes to the "QPRT" nucleic acid or its complement under low stringency conditions,

(xxvi) "S-100 beta" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions,

(xxvii) "SIM TO PLEXIN 1 - MOUSE" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIM TO PLEXIN 1 - MOUSE" encoded by a nucleic acid that hybridizes to the "SIM TO PLEXIN 1 - MOUSE" nucleic acid or its complement under low stringency conditions,

(xxviii) "TGM5" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TGM5" encoded by a nucleic acid that hybridizes to the "TGM5" nucleic acid or its complement under low stringency conditions,

(xxix) "VLDL receptor" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VLDL receptor" encoded by a nucleic acid that hybridizes to the "VLDL receptor" nucleic acid or its complement under low stringency conditions, and/or(xxx) "hypothetical protein FLJ11151" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein FLJ11151" encoded by a nucleic acid that hybridizes to the "hypothetical protein FLJ11151" nucleic acid or its complement under low stringency conditions,as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease;.

The invention further relates to the following embodiments of the JIP1-complex

1. A protein complex selected from complex (I) and comprising

- (a) at least one first protein selected from the group consisting of:
- (i) "APP" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
 - (ii) "ISLET-BRAIN 2" (SEQ ID No:36) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ISLET-BRAIN 2" encoded by a nucleic acid that hybridizes to the "ISLET-BRAIN 2" nucleic acid or its complement under low stringency conditions,
 - (iii) "JIP-1" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "JIP-1" encoded by a nucleic acid that hybridizes to the "JIP-1" nucleic acid or its complement under low stringency conditions, and
 - (iv) "JNK" (SEQ ID No:38) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "JNK" encoded by a nucleic acid that hybridizes to the "JNK" nucleic acid or its complement under low stringency conditions, and
- (b) at least one second protein, which second protein is selected from the group consisting of:
- (i) "ALPHA-CENTRACTIN" (SEQ ID No:31) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ALPHA-CENTRACTIN" encoded by a nucleic acid that hybridizes to the "ALPHA-CENTRACTIN" nucleic acid or its complement under low stringency conditions,
 - (ii) "CASPASE-14 PRECURSOR" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CASPASE-14 PRECURSOR" encoded by a nucleic acid that hybridizes to the "CASPASE-14 PRECURSOR" nucleic acid or its complement under low stringency conditions,
 - (iii) "DCTN1" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DCTN1" encoded by a nucleic acid that hybridizes to the "DCTN1" nucleic acid or its complement under low stringency conditions,
 - (iv) "Dynactin 3, isoform 2" (SEQ ID No:34) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynactin 3,

- isoform 2" encoded by a nucleic acid that hybridizes to the "Dynactin 3, isoform 2" nucleic acid or its complement under low stringency conditions,
- (v) "HARP11, UNCHARACTERIZED HYPOTHALAMUS PROTEIN" (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HARP11, UNCHARACTERIZED HYPOTHALAMUS PROTEIN" encoded by a nucleic acid that hybridizes to the "HARP11, UNCHARACTERIZED HYPOTHALAMUS PROTEIN" nucleic acid or its complement under low stringency conditions,
- (vi) "KINESIN HC" (SEQ ID No:39) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KINESIN HC" encoded by a nucleic acid that hybridizes to the "KINESIN HC" nucleic acid or its complement under low stringency conditions,
- (vii) "KINESIN LC1" (SEQ ID No:40) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KINESIN LC1" encoded by a nucleic acid that hybridizes to the "KINESIN LC1" nucleic acid or its complement under low stringency conditions,
- (viii) "Kif5c" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Kif5c" encoded by a nucleic acid that hybridizes to the "Kif5c" nucleic acid or its complement under low stringency conditions, and
- (ix) "MAPK8IP3/JIP3" (SEQ ID No:21) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MAPK8IP3/JIP3" encoded by a nucleic acid that hybridizes to the "MAPK8IP3/JIP3" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

2. The protein complex according to No. 1 wherein the first protein is the protein Jip1 (SEQ ID NO. 37), or a functionally active derivative thereof, or a functionally active

fragment thereof, or a homolog thereof, or a variant of 'Jip1' encoded by a nucleic acid that hybridizes to the 'Jip1' under low stringency conditions.

3. The protein complex according to No. 1 selected from complex (I) and comprising the following proteins:

- (i) "ALPHA-CENTRACTIN" (SEQ ID No:31) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ALPHA-CENTRACTIN" encoded by a nucleic acid that hybridizes to the "ALPHA-CENTRACTIN" nucleic acid or its complement under low stringency conditions,
- (ii) "APP" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (iii) "CASPASE-14 PRECURSOR" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CASPASE-14 PRECURSOR" encoded by a nucleic acid that hybridizes to the "CASPASE-14 PRECURSOR" nucleic acid or its complement under low stringency conditions,
- (iv) "DCTN1" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DCTN1" encoded by a nucleic acid that hybridizes to the "DCTN1" nucleic acid or its complement under low stringency conditions,
- (v) "Dynactin 3, isoform 2" (SEQ ID No:34) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynactin 3, isoform 2" encoded by a nucleic acid that hybridizes to the "Dynactin 3, isoform 2" nucleic acid or its complement under low stringency conditions,
- (vi) "HARP11, UNCHARACTERIZED HYPOTHALAMUS PROTEIN" (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HARP11, UNCHARACTERIZED HYPOTHALAMUS PROTEIN" encoded by a nucleic acid that hybridizes to the "HARP11, UNCHARACTERIZED HYPOTHALAMUS PROTEIN" nucleic acid or its complement under low stringency conditions,
- (vii) "ISLET-BRAIN 2" (SEQ ID No:36) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ISLET-BRAIN

- 2" encoded by a nucleic acid that hybridizes to the "ISLET-BRAIN 2" nucleic acid or its complement under low stringency conditions,
- (viii) "JIP-1" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "JIP-1" encoded by a nucleic acid that hybridizes to the "JIP-1" nucleic acid or its complement under low stringency conditions,
- (ix) "JNK" (SEQ ID No:38) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "JNK" encoded by a nucleic acid that hybridizes to the "JNK" nucleic acid or its complement under low stringency conditions,
- (x) "KINESIN HC" (SEQ ID No:39) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KINESIN HC" encoded by a nucleic acid that hybridizes to the "KINESIN HC" nucleic acid or its complement under low stringency conditions,
- (xi) "KINESIN LC1" (SEQ ID No:40) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KINESIN LC1" encoded by a nucleic acid that hybridizes to the "KINESIN LC1" nucleic acid or its complement under low stringency conditions,
- (xii) "Kif5c" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Kif5c" encoded by a nucleic acid that hybridizes to the "Kif5c" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "MAPK8IP3/JIP3" (SEQ ID No:21) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MAPK8IP3/JIP3" encoded by a nucleic acid that hybridizes to the "MAPK8IP3/JIP3" nucleic acid or its complement under low stringency conditions,
- and a protein complex selected from complex (II) and comprising the following proteins:
- (i) "ALPHA-CENTRACTIN" (SEQ ID No:31) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ALPHA-CENTRACTIN" encoded by a nucleic acid that hybridizes to the "ALPHA-CENTRACTIN" nucleic acid or its complement under low stringency conditions,
- (ii) "CASPASE-14 PRECURSOR" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CASPASE-14 PRECURSOR" encoded by a nucleic acid that hybridizes to the

"CASPASE-14 PRECURSOR" nucleic acid or its complement under low stringency conditions,

(iii) "DCTN1" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DCTN1" encoded by a nucleic acid that hybridizes to the "DCTN1" nucleic acid or its complement under low stringency conditions,

(iv) "Dynactin 3, isoform 2" (SEQ ID No:34) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynactin 3, isoform 2" encoded by a nucleic acid that hybridizes to the "Dynactin 3, isoform 2" nucleic acid or its complement under low stringency conditions,

(v) "HARP11, UNCHARACTERIZED HYPOTHALAMUS PROTEIN" (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HARP11, UNCHARACTERIZED HYPOTHALAMUS PROTEIN" encoded by a nucleic acid that hybridizes to the "HARP11, UNCHARACTERIZED HYPOTHALAMUS PROTEIN" nucleic acid or its complement under low stringency conditions,

(vi) "ISLET-BRAIN 2" (SEQ ID No:36) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ISLET-BRAIN 2" encoded by a nucleic acid that hybridizes to the "ISLET-BRAIN 2" nucleic acid or its complement under low stringency conditions,

(vii) "JIP-1" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "JIP-1" encoded by a nucleic acid that hybridizes to the "JIP-1" nucleic acid or its complement under low stringency conditions,

(viii) "KINESIN HC" (SEQ ID No:39) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KINESIN HC" encoded by a nucleic acid that hybridizes to the "KINESIN HC" nucleic acid or its complement under low stringency conditions,

(ix) "KINESIN LC1" (SEQ ID No:40) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KINESIN LC1" encoded by a nucleic acid that hybridizes to the "KINESIN LC1" nucleic acid or its complement under low stringency conditions,

(x) "Kif5c" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Kif5c" encoded by a

nucleic acid that hybridizes to the "Kif5c" nucleic acid or its complement under low stringency conditions, and/or

(xi) "MAPK8IP3/JIP3" (SEQ ID No:21) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MAPK8IP3/JIP3" encoded by a nucleic acid that hybridizes to the "MAPK8IP3/JIP3" nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 8 of the following proteins:

- (i) "ALPHA-CENTRACTIN" (SEQ ID No:31) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ALPHA-CENTRACTIN" encoded by a nucleic acid that hybridizes to the "ALPHA-CENTRACTIN" nucleic acid or its complement under low stringency conditions,
- (ii) "APP" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (iii) "CASPASE-14 PRECURSOR" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CASPASE-14 PRECURSOR" encoded by a nucleic acid that hybridizes to the "CASPASE-14 PRECURSOR" nucleic acid or its complement under low stringency conditions,
- (iv) "DCTN1" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DCTN1" encoded by a nucleic acid that hybridizes to the "DCTN1" nucleic acid or its complement under low stringency conditions,
- (v) "Dynactin 3, isoform 2" (SEQ ID No:34) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynactin 3, isoform 2" encoded by a nucleic acid that hybridizes to the "Dynactin 3, isoform 2" nucleic acid or its complement under low stringency conditions,
- (vi) "HARP11, UNCHARACTERIZED HYPOTHALAMUS PROTEIN" (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HARP11, UNCHARACTERIZED HYPOTHALAMUS PROTEIN" encoded by a nucleic acid that hybridizes to the "HARP11,

UNCHARACTERIZED HYPOTHALAMUS PROTEIN" nucleic acid or its complement under low stringency conditions,

(vii) "ISLET-BRAIN 2" (SEQ ID No:36) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ISLET-BRAIN 2" encoded by a nucleic acid that hybridizes to the "ISLET-BRAIN 2" nucleic acid or its complement under low stringency conditions,

(viii) "JIP-1" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "JIP-1" encoded by a nucleic acid that hybridizes to the "JIP-1" nucleic acid or its complement under low stringency conditions,

(ix) "JNK" (SEQ ID No:38) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "JNK" encoded by a nucleic acid that hybridizes to the "JNK" nucleic acid or its complement under low stringency conditions,

(x) "KINESIN HC" (SEQ ID No:39) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KINESIN HC" encoded by a nucleic acid that hybridizes to the "KINESIN HC" nucleic acid or its complement under low stringency conditions,

(xi) "KINESIN LC1" (SEQ ID No:40) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KINESIN LC1" encoded by a nucleic acid that hybridizes to the "KINESIN LC1" nucleic acid or its complement under low stringency conditions,

(xii) "Kif5c" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Kif5c" encoded by a nucleic acid that hybridizes to the "Kif5c" nucleic acid or its complement under low stringency conditions,

(xiii) "MAPK8IP3/JIP3" (SEQ ID No:21) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MAPK8IP3/JIP3" encoded by a nucleic acid that hybridizes to the "MAPK8IP3/JIP3" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the

functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.

6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.

7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.

8. The complex of any of No. 1 - 7 that is involved in the transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).

9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps: expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.

10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.

11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.
12. Component of the JIP1 complex obtainable by a process according to any of No. 9 - 11.
13. Protein of the JIP1 complex selected from
 - (i) "HARP11, UNCHARACTERIZED HYPOTHALAMUS PROTEIN" (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HARP11, UNCHARACTERIZED HYPOTHALAMUS PROTEIN" encoded by a nucleic acid that hybridizes to the "HARP11, UNCHARACTERIZED HYPOTHALAMUS PROTEIN" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.
14. Nucleic acid encoding a protein according to No. 13.
15. Construct, preferably a vector construct, comprising (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or
(b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).

16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).
17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.
18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.
19. The kit according to No. 18 for processing a substrate of said complex.
20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative disease such as Alzheimer's disease and related disorders;.
21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.
22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.
23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:

(i) "HARP11, UNCHARACTERIZED HYPOTHALAMUS PROTEIN" (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HARP11, UNCHARACTERIZED HYPOTHALAMUS PROTEIN" encoded by a nucleic acid that hybridizes to the "HARP11, UNCHARACTERIZED HYPOTHALAMUS PROTEIN" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative disease such as Alzheimer's disease and related disorders;.

25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:

(i) "HARP11, UNCHARACTERIZED HYPOTHALAMUS PROTEIN" (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HARP11, UNCHARACTERIZED HYPOTHALAMUS PROTEIN" encoded by a nucleic acid that hybridizes to the "HARP11, UNCHARACTERIZED HYPOTHALAMUS PROTEIN" nucleic acid or its complement under low stringency conditions, comprising the steps of
(a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and
(b) determinig whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of(a) exposing said complex, or a cell or organism containing JIP1 complex to one or more candidate molecules; and

(b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the

presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.

28. The method of No. 26, wherein the activity of said complex is determined.

29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.

30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.

31. The method of No. 30, wherein said determining step comprises determining whether
(i) "ALPHA-CENTRACTIN" (SEQ ID No:31) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ALPHA-CENTRACTIN" encoded by a nucleic acid that hybridizes to the "ALPHA-CENTRACTIN" nucleic acid or its complement under low stringency conditions, and/or
(ii) "APP" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or
(iii) "CASPASE-14 PRECURSOR" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CASPASE-14 PRECURSOR" encoded by a nucleic acid that hybridizes to the

"CASPASE-14 PRECURSOR" nucleic acid or its complement under low stringency conditions, and/or

- (iv) "DCTN1" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DCTN1" encoded by a nucleic acid that hybridizes to the "DCTN1" nucleic acid or its complement under low stringency conditions, and/or
- (v) "Dynactin 3, isoform 2" (SEQ ID No:34) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynactin 3, isoform 2" encoded by a nucleic acid that hybridizes to the "Dynactin 3, isoform 2" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "HARP11, UNCHARACTERIZED HYPOTHALAMUS PROTEIN" (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HARP11, UNCHARACTERIZED HYPOTHALAMUS PROTEIN" encoded by a nucleic acid that hybridizes to the "HARP11, UNCHARACTERIZED HYPOTHALAMUS PROTEIN" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "ISLET-BRAIN 2" (SEQ ID No:36) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ISLET-BRAIN 2" encoded by a nucleic acid that hybridizes to the "ISLET-BRAIN 2" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "JIP-1" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "JIP-1" encoded by a nucleic acid that hybridizes to the "JIP-1" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "JNK" (SEQ ID No:38) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "JNK" encoded by a nucleic acid that hybridizes to the "JNK" nucleic acid or its complement under low stringency conditions, and/or
- (x) "KINESIN HC" (SEQ ID No:39) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KINESIN HC" encoded by a nucleic acid that hybridizes to the "KINESIN HC" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "KINESIN LC1" (SEQ ID No:40) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KINESIN LC1"

encoded by a nucleic acid that hybridizes to the "KINESIN LC1" nucleic acid or its complement under low stringency conditions, and/or

(xii) "Kif5c" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Kif5c" encoded by a nucleic acid that hybridizes to the "Kif5c" nucleic acid or its complement under low stringency conditions, and/or

(xiii) "MAPK8IP3/JIP3" (SEQ ID No:21) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MAPK8IP3/JIP3" encoded by a nucleic acid that hybridizes to the "MAPK8IP3/JIP3" nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease and related disorders;.

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease and related disorders;.

34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a

comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.
37. The method of No. 35, wherein the activity of said complex is determined.
38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.
39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.
40. The method of No. 39, wherein said determining step comprises determining whether
 - (i) "ALPHA-CENTRACTIN" (SEQ ID No:31) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ALPHA-CENTRACTIN" encoded by a nucleic acid that hybridizes to the "ALPHA-CENTRACTIN" nucleic acid or its complement under low stringency conditions, and/or
 - (ii) "APP" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or
 - (iii) "CASPASE-14 PRECURSOR" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CASPASE-14 PRECURSOR" encoded by a nucleic acid that hybridizes to the "CASPASE-14 PRECURSOR" nucleic acid or its complement under low stringency conditions, and/or

- (iv) "DCTN1" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DCTN1" encoded by a nucleic acid that hybridizes to the "DCTN1" nucleic acid or its complement under low stringency conditions, and/or
- (v) "Dynactin 3, isoform 2" (SEQ ID No:34) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynactin 3, isoform 2" encoded by a nucleic acid that hybridizes to the "Dynactin 3, isoform 2" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "HARP11, UNCHARACTERIZED HYPOTHALAMUS PROTEIN" (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HARP11, UNCHARACTERIZED HYPOTHALAMUS PROTEIN" encoded by a nucleic acid that hybridizes to the "HARP11, UNCHARACTERIZED HYPOTHALAMUS PROTEIN" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "ISLET-BRAIN 2" (SEQ ID No:36) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ISLET-BRAIN 2" encoded by a nucleic acid that hybridizes to the "ISLET-BRAIN 2" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "JIP-1" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "JIP-1" encoded by a nucleic acid that hybridizes to the "JIP-1" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "JNK" (SEQ ID No:38) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "JNK" encoded by a nucleic acid that hybridizes to the "JNK" nucleic acid or its complement under low stringency conditions, and/or
- (x) "KINESIN HC" (SEQ ID No:39) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KINESIN HC" encoded by a nucleic acid that hybridizes to the "KINESIN HC" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "KINESIN LC1" (SEQ ID No:40) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KINESIN LC1" encoded by a nucleic acid that hybridizes to the "KINESIN LC1" nucleic acid or its complement under low stringency conditions, and/or

- (xii) "Kif5c" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Kif5c" encoded by a nucleic acid that hybridizes to the "Kif5c" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "MAPK8IP3/JIP3" (SEQ ID No:21) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MAPK8IP3/JIP3" encoded by a nucleic acid that hybridizes to the "MAPK8IP3/JIP3" nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative disease such as Alzheimer's disease and related disorders;.
42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.
43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42 , wherein said disease or disorder involves increased levels of the amount or activity of said complex.
45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins
- (i) "ALPHA-CENTRACTIN" (SEQ ID No:31) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ALPHA-CENTRACTIN" encoded by a nucleic acid that hybridizes to the "ALPHA-CENTRACTIN" nucleic acid or its complement under low stringency conditions,
 - (ii) "APP" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
 - (iii) "CASPASE-14 PRECURSOR" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CASPASE-14 PRECURSOR" encoded by a nucleic acid that hybridizes to the "CASPASE-14 PRECURSOR" nucleic acid or its complement under low stringency conditions,
 - (iv) "DCTN1" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DCTN1" encoded by a nucleic acid that hybridizes to the "DCTN1" nucleic acid or its complement under low stringency conditions,
 - (v) "Dynactin 3, isoform 2" (SEQ ID No:34) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynactin 3, isoform 2" encoded by a nucleic acid that hybridizes to the "Dynactin 3, isoform 2" nucleic acid or its complement under low stringency conditions,
 - (vi) "HARP11, UNCHARACTERIZED HYPOTHALAMUS PROTEIN" (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HARP11, UNCHARACTERIZED HYPOTHALAMUS PROTEIN" encoded by a nucleic acid that hybridizes to the "HARP11, UNCHARACTERIZED HYPOTHALAMUS PROTEIN" nucleic acid or its complement under low stringency conditions,
 - (vii) "ISLET-BRAIN 2" (SEQ ID No:36) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ISLET-BRAIN

2" encoded by a nucleic acid that hybridizes to the "ISLET-BRAIN 2" nucleic acid or its complement under low stringency conditions,

(viii) "JIP-1" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "JIP-1" encoded by a nucleic acid that hybridizes to the "JIP-1" nucleic acid or its complement under low stringency conditions,

(ix) "JNK" (SEQ ID No:38) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "JNK" encoded by a nucleic acid that hybridizes to the "JNK" nucleic acid or its complement under low stringency conditions,

(x) "KINESIN HC" (SEQ ID No:39) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KINESIN HC" encoded by a nucleic acid that hybridizes to the "KINESIN HC" nucleic acid or its complement under low stringency conditions,

(xi) "KINESIN LC1" (SEQ ID No:40) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KINESIN LC1" encoded by a nucleic acid that hybridizes to the "KINESIN LC1" nucleic acid or its complement under low stringency conditions,

(xii) "Kif5c" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Kif5c" encoded by a nucleic acid that hybridizes to the "Kif5c" nucleic acid or its complement under low stringency conditions, and/or(xiii) "MAPK8IP3/JIP3" (SEQ ID No:21) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MAPK8IP3/JIP3" encoded by a nucleic acid that hybridizes to the "MAPK8IP3/JIP3" nucleic acid or its complement under low stringency conditions,as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease and related disorders;.

The invention further relates to the following embodiments of the Fe65L2-complex

1. A protein complex selected from complex (I) and comprising
 - (a) at least one first protein selected from the group consisting of:

- (i) "APLP1" (SEQ ID No:42) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,
 - (ii) "APLP2" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,
 - (iii) "APP" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and
 - (iv) "Fe65L2" (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L2" encoded by a nucleic acid that hybridizes to the "Fe65L2" nucleic acid or its complement under low stringency conditions, and
- (b) at least one second protein, which second protein is selected from the group consisting of:
- (i) "CDC42BPB" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDC42BPB" encoded by a nucleic acid that hybridizes to the "CDC42BPB" nucleic acid or its complement under low stringency conditions,
 - (ii) "COP9" (SEQ ID No:44) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COP9" encoded by a nucleic acid that hybridizes to the "COP9" nucleic acid or its complement under low stringency conditions,
 - (iii) "COP9 COMPLEX SUBUNIT 4" (SEQ ID No:45) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COP9 COMPLEX SUBUNIT 4" encoded by a nucleic acid that hybridizes to the "COP9 COMPLEX SUBUNIT 4" nucleic acid or its complement under low stringency conditions,
 - (iv) "COP9 complex subunit 7a" (SEQ ID No:46) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COP9 complex subunit 7a" encoded by a nucleic acid that hybridizes to the "COP9 complex subunit 7a" nucleic acid or its complement under low stringency conditions,

- (v) "COPS3" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPS3" encoded by a nucleic acid that hybridizes to the "COPS3" nucleic acid or its complement under low stringency conditions,
- (vi) "COPS5" (SEQ ID No:48) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPS5" encoded by a nucleic acid that hybridizes to the "COPS5" nucleic acid or its complement under low stringency conditions,
- (vii) "COPS6: COP9 subunit 6 (MOV34 homolog, 34 kD)" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPS6: COP9 subunit 6 (MOV34 homolog, 34 kD)" encoded by a nucleic acid that hybridizes to the "COPS6: COP9 subunit 6 (MOV34 homolog, 34 kD)" nucleic acid or its complement under low stringency conditions,
- (viii) "COPS7B" (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPS7B" encoded by a nucleic acid that hybridizes to the "COPS7B" nucleic acid or its complement under low stringency conditions,
- (ix) "CUL3" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CUL3" encoded by a nucleic acid that hybridizes to the "CUL3" nucleic acid or its complement under low stringency conditions,
- (x) "Contactin1" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Contactin1" encoded by a nucleic acid that hybridizes to the "Contactin1" nucleic acid or its complement under low stringency conditions,
- (xi) "FLJ12599" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ12599" encoded by a nucleic acid that hybridizes to the "FLJ12599" nucleic acid or its complement under low stringency conditions,
- (xii) "GPR49" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPR49" encoded by a nucleic acid that hybridizes to the "GPR49" nucleic acid or its complement under low stringency conditions,

- (xiii) "GPS1" (SEQ ID No:55) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPS1" encoded by a nucleic acid that hybridizes to the "GPS1" nucleic acid or its complement under low stringency conditions,
- (xiv) "KIAA1102 PROTEIN (FRAGMENT)" (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1102 PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xv) "NEDD8" (SEQ ID No:57) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEDD8" encoded by a nucleic acid that hybridizes to the "NEDD8" nucleic acid or its complement under low stringency conditions,
- (xvi) "Protocadherin gamma C3" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin gamma C3" encoded by a nucleic acid that hybridizes to the "Protocadherin gamma C3" nucleic acid or its complement under low stringency conditions,
- (xvii) "RBX1" (SEQ ID No:59) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RBX1" encoded by a nucleic acid that hybridizes to the "RBX1" nucleic acid or its complement under low stringency conditions,
- (xviii) "RHOBTB1" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RHOBTB1" encoded by a nucleic acid that hybridizes to the "RHOBTB1" nucleic acid or its complement under low stringency conditions,
- (xix) "RHOBTB2" (SEQ ID No:61) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RHOBTB2" encoded by a nucleic acid that hybridizes to the "RHOBTB2" nucleic acid or its complement under low stringency conditions,
- (xx) "SIM TO CGI-20" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIM TO CGI-20" encoded by a nucleic acid that hybridizes to the "SIM TO CGI-20" nucleic acid or its complement under low stringency conditions,

(xxi) "SIMILAR TO POL POLYPROTEIN" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO POL POLYPROTEIN" encoded by a nucleic acid that hybridizes to the "SIMILAR TO POL POLYPROTEIN" nucleic acid or its complement under low stringency conditions,

(xxii) "TRIP15" (SEQ ID No:64) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TRIP15" encoded by a nucleic acid that hybridizes to the "TRIP15" nucleic acid or its complement under low stringency conditions,

(xxiii) "TUBGCP3" (SEQ ID No:65) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TUBGCP3" encoded by a nucleic acid that hybridizes to the "TUBGCP3" nucleic acid or its complement under low stringency conditions, and

(xxiv) "USP11" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "USP11" encoded by a nucleic acid that hybridizes to the "USP11" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

2. The protein complex according to No. 1 wherein the first protein is the protein Fe65L2 (SEQ ID NO. 53), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of 'Fe65L2' encoded by a nucleic acid that hybridizes to the 'Fe65L2' under low stringency conditions.

3. The protein complex according to No. 1 selected from complex (I) and comprising the following proteins:

(i) "APLP1" (SEQ ID No:42) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a

nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,

- (ii) "APLP2" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,
- (iii) "APP" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (iv) "CDC42BPB" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDC42BPB" encoded by a nucleic acid that hybridizes to the "CDC42BPB" nucleic acid or its complement under low stringency conditions,
- (v) "COP9" (SEQ ID No:44) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COP9" encoded by a nucleic acid that hybridizes to the "COP9" nucleic acid or its complement under low stringency conditions,
- (vi) "COP9 COMPLEX SUBUNIT 4" (SEQ ID No:45) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COP9 COMPLEX SUBUNIT 4" encoded by a nucleic acid that hybridizes to the "COP9 COMPLEX SUBUNIT 4" nucleic acid or its complement under low stringency conditions,
- (vii) "COP9 complex subunit 7a" (SEQ ID No:46) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COP9 complex subunit 7a" encoded by a nucleic acid that hybridizes to the "COP9 complex subunit 7a" nucleic acid or its complement under low stringency conditions,
- (viii) "COPS3" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPS3" encoded by a nucleic acid that hybridizes to the "COPS3" nucleic acid or its complement under low stringency conditions,
- (ix) "COPS5" (SEQ ID No:48) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPS5" encoded by a nucleic acid that hybridizes to the "COPS5" nucleic acid or its complement under low stringency conditions,

- (x) "COPS6: COP9 subunit 6 (MOV34 homolog, 34 kD)" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPS6: COP9 subunit 6 (MOV34 homolog, 34 kD)" encoded by a nucleic acid that hybridizes to the "COPS6: COP9 subunit 6 (MOV34 homolog, 34 kD)" nucleic acid or its complement under low stringency conditions,
- (xi) "COPS7B" (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPS7B" encoded by a nucleic acid that hybridizes to the "COPS7B" nucleic acid or its complement under low stringency conditions,
- (xii) "CUL3" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CUL3" encoded by a nucleic acid that hybridizes to the "CUL3" nucleic acid or its complement under low stringency conditions,
- (xiii) "Contactin1" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Contactin1" encoded by a nucleic acid that hybridizes to the "Contactin1" nucleic acid or its complement under low stringency conditions,
- (xiv) "FLJ12599" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ12599" encoded by a nucleic acid that hybridizes to the "FLJ12599" nucleic acid or its complement under low stringency conditions,
- (xv) "Fe65L2" (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L2" encoded by a nucleic acid that hybridizes to the "Fe65L2" nucleic acid or its complement under low stringency conditions,
- (xvi) "GPR49" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPR49" encoded by a nucleic acid that hybridizes to the "GPR49" nucleic acid or its complement under low stringency conditions,
- (xvii) "GPS1" (SEQ ID No:55) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPS1" encoded by a nucleic acid that hybridizes to the "GPS1" nucleic acid or its complement under low stringency conditions,

- (xviii) "KIAA1102 PROTEIN (FRAGMENT)" (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1102 PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xix) "NEDD8" (SEQ ID No:57) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEDD8" encoded by a nucleic acid that hybridizes to the "NEDD8" nucleic acid or its complement under low stringency conditions,
- (xx) "Protocadherin gamma C3" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin gamma C3" encoded by a nucleic acid that hybridizes to the "Protocadherin gamma C3" nucleic acid or its complement under low stringency conditions,
- (xxi) "RBX1" (SEQ ID No:59) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RBX1" encoded by a nucleic acid that hybridizes to the "RBX1" nucleic acid or its complement under low stringency conditions,
- (xxii) "RHOBTB1" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RHOBTB1" encoded by a nucleic acid that hybridizes to the "RHOBTB1" nucleic acid or its complement under low stringency conditions,
- (xxiii) "RHOBTB2" (SEQ ID No:61) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RHOBTB2" encoded by a nucleic acid that hybridizes to the "RHOBTB2" nucleic acid or its complement under low stringency conditions,
- (xxiv) "SIM TO CGI-20" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIM TO CGI-20" encoded by a nucleic acid that hybridizes to the "SIM TO CGI-20" nucleic acid or its complement under low stringency conditions,
- (xxv) "SIMILAR TO POL POLYPYPROTEIN" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO POL POLYPYPROTEIN" encoded by a nucleic acid that hybridizes

to the "SIMILAR TO POL POLYPROTEIN" nucleic acid or its complement under low stringency conditions,

(xxvi) "TRIP15" (SEQ ID No:64) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TRIP15" encoded by a nucleic acid that hybridizes to the "TRIP15" nucleic acid or its complement under low stringency conditions,

(xxvii) "TUBGCP3" (SEQ ID No:65) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TUBGCP3" encoded by a nucleic acid that hybridizes to the "TUBGCP3" nucleic acid or its complement under low stringency conditions, and/or

(xxviii) "USP11" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "USP11" encoded by a nucleic acid that hybridizes to the "USP11" nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 23 of the following proteins:

(i) "APLP1" (SEQ ID No:42) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,

(ii) "APLP2" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,

(iii) "APP" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,

(iv) "CDC42BPB" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDC42BPB" encoded by a nucleic acid that hybridizes to the "CDC42BPB" nucleic acid or its complement under low stringency conditions,

- (v) "COP9" (SEQ ID No:44) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COP9" encoded by a nucleic acid that hybridizes to the "COP9" nucleic acid or its complement under low stringency conditions,
- (vi) "COP9 COMPLEX SUBUNIT 4" (SEQ ID No:45) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COP9 COMPLEX SUBUNIT 4" encoded by a nucleic acid that hybridizes to the "COP9 COMPLEX SUBUNIT 4" nucleic acid or its complement under low stringency conditions,
- (vii) "COP9 complex subunit 7a" (SEQ ID No:46) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COP9 complex subunit 7a" encoded by a nucleic acid that hybridizes to the "COP9 complex subunit 7a" nucleic acid or its complement under low stringency conditions,
- (viii) "COPS3" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPS3" encoded by a nucleic acid that hybridizes to the "COPS3" nucleic acid or its complement under low stringency conditions,
- (ix) "COPS5" (SEQ ID No:48) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPS5" encoded by a nucleic acid that hybridizes to the "COPS5" nucleic acid or its complement under low stringency conditions,
- (x) "COPS6: COP9 subunit 6 (MOV34 homolog, 34 kD)" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPS6: COP9 subunit 6 (MOV34 homolog, 34 kD)" encoded by a nucleic acid that hybridizes to the "COPS6: COP9 subunit 6 (MOV34 homolog, 34 kD)" nucleic acid or its complement under low stringency conditions,
- (xi) "COPS7B" (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPS7B" encoded by a nucleic acid that hybridizes to the "COPS7B" nucleic acid or its complement under low stringency conditions,
- (xii) "CUL3" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CUL3" encoded by a nucleic acid that hybridizes to the "CUL3" nucleic acid or its complement under low stringency conditions,

- (xiii) "Contactin1" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Contactin1" encoded by a nucleic acid that hybridizes to the "Contactin1" nucleic acid or its complement under low stringency conditions,
- (xiv) "FLJ12599" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ12599" encoded by a nucleic acid that hybridizes to the "FLJ12599" nucleic acid or its complement under low stringency conditions,
- (xv) "Fe65L2" (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L2" encoded by a nucleic acid that hybridizes to the "Fe65L2" nucleic acid or its complement under low stringency conditions,
- (xvi) "GPR49" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPR49" encoded by a nucleic acid that hybridizes to the "GPR49" nucleic acid or its complement under low stringency conditions,
- (xvii) "GPS1" (SEQ ID No:55) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPS1" encoded by a nucleic acid that hybridizes to the "GPS1" nucleic acid or its complement under low stringency conditions,
- (xviii) "KIAA1102 PROTEIN (FRAGMENT)" (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1102 PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xix) "NEDD8" (SEQ ID No:57) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEDD8" encoded by a nucleic acid that hybridizes to the "NEDD8" nucleic acid or its complement under low stringency conditions,
- (xx) "Protocadherin gamma C3" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin gamma C3" encoded by a nucleic acid that hybridizes to the "Protocadherin gamma C3" nucleic acid or its complement under low stringency conditions,

- (xxi) "RBX1" (SEQ ID No:59) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RBX1" encoded by a nucleic acid that hybridizes to the "RBX1" nucleic acid or its complement under low stringency conditions,
- (xxii) "RHOBTB1" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RHOBTB1" encoded by a nucleic acid that hybridizes to the "RHOBTB1" nucleic acid or its complement under low stringency conditions,
- (xxiii) "RHOBTB2" (SEQ ID No:61) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RHOBTB2" encoded by a nucleic acid that hybridizes to the "RHOBTB2" nucleic acid or its complement under low stringency conditions,
- (xxiv) "SIM TO CGI-20" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIM TO CGI-20" encoded by a nucleic acid that hybridizes to the "SIM TO CGI-20" nucleic acid or its complement under low stringency conditions,
- (xxv) "SIMILAR TO POL POLYPROTEIN" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO POL POLYPROTEIN" encoded by a nucleic acid that hybridizes to the "SIMILAR TO POL POLYPROTEIN" nucleic acid or its complement under low stringency conditions,
- (xxvi) "TRIP15" (SEQ ID No:64) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TRIP15" encoded by a nucleic acid that hybridizes to the "TRIP15" nucleic acid or its complement under low stringency conditions,
- (xxvii) "TUBGCP3" (SEQ ID No:65) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TUBGCP3" encoded by a nucleic acid that hybridizes to the "TUBGCP3" nucleic acid or its complement under low stringency conditions,
- (xxviii) "USP11" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "USP11" encoded by a nucleic acid that hybridizes to the "USP11" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.
6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.
7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.
8. The complex of any of No. 1 - 7 that is involved in the transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).
9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps: expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.

10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.
11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.
12. Component of the Fe65L2 obtainable by a process according to any of No. 9 - 11.
13. Protein of the Fe65L2 selected from
 - (i) "FLJ12599" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ12599" encoded by a nucleic acid that hybridizes to the "FLJ12599" nucleic acid or its complement under low stringency conditions,
 - (ii) "GPR49" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPR49" encoded by a nucleic acid that hybridizes to the "GPR49" nucleic acid or its complement under low stringency conditions,
 - (iii) "KIAA1102 PROTEIN (FRAGMENT)" (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1102 PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
 - (iv) "Protocadherin gamma C3" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin gamma C3" encoded by a nucleic acid that hybridizes to the "Protocadherin gamma C3" nucleic acid or its complement under low stringency conditions,
 - (v) "RHOBTB1" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RHOBTB1" encoded by a nucleic acid that hybridizes to the "RHOBTB1" nucleic acid or its complement under low stringency conditions,
 - (vi) "RHOBTB2" (SEQ ID No:61) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RHOBTB2"

encoded by a nucleic acid that hybridizes to the "RHOBTB2" nucleic acid or its complement under low stringency conditions,

(vii) "SIM TO CGI-20" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIM TO CGI-20" encoded by a nucleic acid that hybridizes to the "SIM TO CGI-20" nucleic acid or its complement under low stringency conditions,

(viii) "SIMILAR TO POL POLYPYROTEIN" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO POL POLYPYROTEIN" encoded by a nucleic acid that hybridizes to the "SIMILAR TO POL POLYPYROTEIN" nucleic acid or its complement under low stringency conditions, and

(ix) "USP11" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "USP11" encoded by a nucleic acid that hybridizes to the "USP11" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

14. Nucleic acid encoding a protein according to No. 13.

15. Construct, preferably a vector construct, comprising (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or

(b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).

16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).
17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.
18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.
19. The kit according to No. 18 for processing a substrate of said complex.
20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; cancer such as prostate cancer and breast cancer and skin cancer .
21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.
22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.

23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:

- (i) "FLJ12599" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ12599" encoded by a nucleic acid that hybridizes to the "FLJ12599" nucleic acid or its complement under low stringency conditions,
- (ii) "GPR49" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPR49" encoded by a nucleic acid that hybridizes to the "GPR49" nucleic acid or its complement under low stringency conditions,
- (iii) "KIAA1102 PROTEIN (FRAGMENT)" (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1102 PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (iv) "Protocadherin gamma C3" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin gamma C3" encoded by a nucleic acid that hybridizes to the "Protocadherin gamma C3" nucleic acid or its complement under low stringency conditions,
- (v) "RHOBTB1" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RHOBTB1" encoded by a nucleic acid that hybridizes to the "RHOBTB1" nucleic acid or its complement under low stringency conditions,
- (vi) "RHOBTB2" (SEQ ID No:61) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RHOBTB2" encoded by a nucleic acid that hybridizes to the "RHOBTB2" nucleic acid or its complement under low stringency conditions,
- (vii) "SIM TO CGI-20" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIM TO CGI-20" encoded by a nucleic acid that hybridizes to the "SIM TO CGI-20" nucleic acid or its complement under low stringency conditions,
- (viii) "SIMILAR TO POL POLYPROTEIN" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a

variant of "SIMILAR TO POL POLYPROTEIN" encoded by a nucleic acid that hybridizes to the "SIMILAR TO POL POLYPROTEIN" nucleic acid or its complement under low stringency conditions, and/or

(ix) "USP11" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "USP11" encoded by a nucleic acid that hybridizes to the "USP11" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative disease such as Alzheimer's disease; cancer such as prostate cancer and breast cancer and skin cancer .

25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:

- (i) "FLJ12599" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ12599" encoded by a nucleic acid that hybridizes to the "FLJ12599" nucleic acid or its complement under low stringency conditions,
- (ii) "GPR49" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPR49" encoded by a nucleic acid that hybridizes to the "GPR49" nucleic acid or its complement under low stringency conditions,
- (iii) "KIAA1102 PROTEIN (FRAGMENT)" (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1102 PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (iv) "Protocadherin gamma C3" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin gamma C3" encoded by a nucleic acid that hybridizes to the "Protocadherin gamma C3" nucleic acid or its complement under low stringency conditions,

- (v) "RHOBTB1" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RHOBTB1" encoded by a nucleic acid that hybridizes to the "RHOBTB1" nucleic acid or its complement under low stringency conditions,
- (vi) "RHOBTB2" (SEQ ID No:61) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RHOBTB2" encoded by a nucleic acid that hybridizes to the "RHOBTB2" nucleic acid or its complement under low stringency conditions,
- (vii) "SIM TO CGI-20" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIM TO CGI-20" encoded by a nucleic acid that hybridizes to the "SIM TO CGI-20" nucleic acid or its complement under low stringency conditions,
- (viii) "SIMILAR TO POL POLYPYROTEIN" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO POL POLYPYROTEIN" encoded by a nucleic acid that hybridizes to the "SIMILAR TO POL POLYPYROTEIN" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "USP11" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "USP11" encoded by a nucleic acid that hybridizes to the "USP11" nucleic acid or its complement under low stringency conditions, comprising the steps of
 - (a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and
 - (b) determining whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of
- (a) exposing said complex, or a cell or organism containing Fe65L2 to one or more candidate molecules; and
 - (b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the

presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.

28. The method of No. 26, wherein the activity of said complex is determined.

29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.

30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.

31. The method of No. 30, wherein said determining step comprises determining whether

(i) "APLP1" (SEQ ID No:42) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions, and/or

(ii) "APLP2" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions, and/or

(iii) "APP" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or

- (iv) "CDC42BPB" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDC42BPB" encoded by a nucleic acid that hybridizes to the "CDC42BPB" nucleic acid or its complement under low stringency conditions, and/or
- (v) "COP9" (SEQ ID No:44) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COP9" encoded by a nucleic acid that hybridizes to the "COP9" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "COP9 COMPLEX SUBUNIT 4" (SEQ ID No:45) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COP9 COMPLEX SUBUNIT 4" encoded by a nucleic acid that hybridizes to the "COP9 COMPLEX SUBUNIT 4" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "COP9 complex subunit 7a" (SEQ ID No:46) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COP9 complex subunit 7a" encoded by a nucleic acid that hybridizes to the "COP9 complex subunit 7a" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "COPS3" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPS3" encoded by a nucleic acid that hybridizes to the "COPS3" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "COPS5" (SEQ ID No:48) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPS5" encoded by a nucleic acid that hybridizes to the "COPS5" nucleic acid or its complement under low stringency conditions, and/or
- (x) "COPS6: COP9 subunit 6 (MOV34 homolog, 34 kD)" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPS6: COP9 subunit 6 (MOV34 homolog, 34 kD)" encoded by a nucleic acid that hybridizes to the "COPS6: COP9 subunit 6 (MOV34 homolog, 34 kD)" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "COPS7B" (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPS7B" encoded by a

nucleic acid that hybridizes to the "COPS7B" nucleic acid or its complement under low stringency conditions, and/or

(xii) "CUL3" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CUL3" encoded by a nucleic acid that hybridizes to the "CUL3" nucleic acid or its complement under low stringency conditions, and/or

(xiii) "Contactin1" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Contactin1" encoded by a nucleic acid that hybridizes to the "Contactin1" nucleic acid or its complement under low stringency conditions, and/or

(xiv) "FLJ12599" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ12599" encoded by a nucleic acid that hybridizes to the "FLJ12599" nucleic acid or its complement under low stringency conditions, and/or

(xv) "Fe65L2" (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L2" encoded by a nucleic acid that hybridizes to the "Fe65L2" nucleic acid or its complement under low stringency conditions, and/or

(xvi) "GPR49" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPR49" encoded by a nucleic acid that hybridizes to the "GPR49" nucleic acid or its complement under low stringency conditions, and/or

(xvii) "GPS1" (SEQ ID No:55) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPS1" encoded by a nucleic acid that hybridizes to the "GPS1" nucleic acid or its complement under low stringency conditions, and/or

(xviii) "KIAA1102 PROTEIN (FRAGMENT)" (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1102 PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or

(xix) "NEDD8" (SEQ ID No:57) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEDD8" encoded by a

nucleic acid that hybridizes to the "NEDD8" nucleic acid or its complement under low stringency conditions, and/or

(xx) "Protocadherin gamma C3" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin gamma C3" encoded by a nucleic acid that hybridizes to the "Protocadherin gamma C3" nucleic acid or its complement under low stringency conditions, and/or

(xxi) "RBX1" (SEQ ID No:59) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RBX1" encoded by a nucleic acid that hybridizes to the "RBX1" nucleic acid or its complement under low stringency conditions, and/or

(xxii) "RHOBTB1" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RHOBTB1" encoded by a nucleic acid that hybridizes to the "RHOBTB1" nucleic acid or its complement under low stringency conditions, and/or

(xxiii) "RHOBTB2" (SEQ ID No:61) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RHOBTB2" encoded by a nucleic acid that hybridizes to the "RHOBTB2" nucleic acid or its complement under low stringency conditions, and/or

(xxiv) "SIM TO CGI-20" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIM TO CGI-20" encoded by a nucleic acid that hybridizes to the "SIM TO CGI-20" nucleic acid or its complement under low stringency conditions, and/or

(xxv) "SIMILAR TO POL POLYPROTEIN" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO POL POLYPROTEIN" encoded by a nucleic acid that hybridizes to the "SIMILAR TO POL POLYPROTEIN" nucleic acid or its complement under low stringency conditions, and/or

(xxvi) "TRIP15" (SEQ ID No:64) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TRIP15" encoded by a nucleic acid that hybridizes to the "TRIP15" nucleic acid or its complement under low stringency conditions, and/or

(xxvii) "TUBGCP3" (SEQ ID No:65) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TUBGCP3"

encoded by a nucleic acid that hybridizes to the "TUBGCP3" nucleic acid or its complement under low stringency conditions, and/or
(xxviii) "USP11" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "USP11" encoded by a nucleic acid that hybridizes to the "USP11" nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; cancer such as prostate cancer and breast cancer and skin cancer .

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; cancer such as prostate cancer and breast cancer and skin cancer .

34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not

having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.

37. The method of No. 35, wherein the activity of said complex is determined.

38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

40. The method of No. 39, wherein said determining step comprises determining whether

(i) "APLP1" (SEQ ID No:42) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions, and/or

(ii) "APLP2" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions, and/or

(iii) "APP" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or

(iv) "CDC42BPB" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDC42BPB" encoded by a nucleic acid that hybridizes to the "CDC42BPB" nucleic acid or its complement under low stringency conditions, and/or

- (v) "COP9" (SEQ ID No:44) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COP9" encoded by a nucleic acid that hybridizes to the "COP9" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "COP9 COMPLEX SUBUNIT 4" (SEQ ID No:45) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COP9 COMPLEX SUBUNIT 4" encoded by a nucleic acid that hybridizes to the "COP9 COMPLEX SUBUNIT 4" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "COP9 complex subunit 7a" (SEQ ID No:46) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COP9 complex subunit 7a" encoded by a nucleic acid that hybridizes to the "COP9 complex subunit 7a" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "COPS3" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPS3" encoded by a nucleic acid that hybridizes to the "COPS3" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "COPS5" (SEQ ID No:48) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPS5" encoded by a nucleic acid that hybridizes to the "COPS5" nucleic acid or its complement under low stringency conditions, and/or
- (x) "COPS6: COP9 subunit 6 (MOV34 homolog, 34 kD)" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPS6: COP9 subunit 6 (MOV34 homolog, 34 kD)" encoded by a nucleic acid that hybridizes to the "COPS6: COP9 subunit 6 (MOV34 homolog, 34 kD)" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "COPS7B" (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPS7B" encoded by a nucleic acid that hybridizes to the "COPS7B" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "CUL3" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CUL3" encoded by a

nucleic acid that hybridizes to the "CUL3" nucleic acid or its complement under low stringency conditions, and/or

(xiii) "Contactin1" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Contactin1" encoded by a nucleic acid that hybridizes to the "Contactin1" nucleic acid or its complement under low stringency conditions, and/or

(xiv) "FLJ12599" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ12599" encoded by a nucleic acid that hybridizes to the "FLJ12599" nucleic acid or its complement under low stringency conditions, and/or

(xv) "Fe65L2" (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L2" encoded by a nucleic acid that hybridizes to the "Fe65L2" nucleic acid or its complement under low stringency conditions, and/or

(xvi) "GPR49" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPR49" encoded by a nucleic acid that hybridizes to the "GPR49" nucleic acid or its complement under low stringency conditions, and/or

(xvii) "GPS1" (SEQ ID No:55) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPS1" encoded by a nucleic acid that hybridizes to the "GPS1" nucleic acid or its complement under low stringency conditions, and/or

(xviii) "KIAA1102 PROTEIN (FRAGMENT)" (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1102 PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or

(xix) "NEDD8" (SEQ ID No:57) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEDD8" encoded by a nucleic acid that hybridizes to the "NEDD8" nucleic acid or its complement under low stringency conditions, and/or

(xx) "Protocadherin gamma C3" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin gamma C3" encoded by a nucleic acid that hybridizes to the

"Protocadherin gamma C3" nucleic acid or its complement under low stringency conditions, and/or

(xxi) "RBX1" (SEQ ID No:59) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RBX1" encoded by a nucleic acid that hybridizes to the "RBX1" nucleic acid or its complement under low stringency conditions, and/or

(xxii) "RHOBTB1" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RHOBTB1" encoded by a nucleic acid that hybridizes to the "RHOBTB1" nucleic acid or its complement under low stringency conditions, and/or

(xxiii) "RHOBTB2" (SEQ ID No:61) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RHOBTB2" encoded by a nucleic acid that hybridizes to the "RHOBTB2" nucleic acid or its complement under low stringency conditions, and/or

(xxiv) "SIM TO CGI-20" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIM TO CGI-20" encoded by a nucleic acid that hybridizes to the "SIM TO CGI-20" nucleic acid or its complement under low stringency conditions, and/or

(xxv) "SIMILAR TO POL POLYPROTEIN" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO POL POLYPROTEIN" encoded by a nucleic acid that hybridizes to the "SIMILAR TO POL POLYPROTEIN" nucleic acid or its complement under low stringency conditions, and/or

(xxvi) "TRIP15" (SEQ ID No:64) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TRIP15" encoded by a nucleic acid that hybridizes to the "TRIP15" nucleic acid or its complement under low stringency conditions, and/or

(xxvii) "TUBGCP3" (SEQ ID No:65) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TUBGCP3" encoded by a nucleic acid that hybridizes to the "TUBGCP3" nucleic acid or its complement under low stringency conditions, and/or

(xxviii) "USP11" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "USP11"

encoded by a nucleic acid that hybridizes to the "USP11" nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; cancer such as prostate cancer and breast cancer and skin cancer .

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42 , wherein said disease or disorder involves increased levels of the amount or activity of said complex.

45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins

- (i) "APLP1" (SEQ ID No:42) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,
- (ii) "APLP2" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,
- (iii) "APP" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (iv) "CDC42BPB" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDC42BPB" encoded by a nucleic acid that hybridizes to the "CDC42BPB" nucleic acid or its complement under low stringency conditions,
- (v) "COP9" (SEQ ID No:44) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COP9" encoded by a nucleic acid that hybridizes to the "COP9" nucleic acid or its complement under low stringency conditions,
- (vi) "COP9 COMPLEX SUBUNIT 4" (SEQ ID No:45) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COP9 COMPLEX SUBUNIT 4" encoded by a nucleic acid that hybridizes to the "COP9 COMPLEX SUBUNIT 4" nucleic acid or its complement under low stringency conditions,
- (vii) "COP9 complex subunit 7a" (SEQ ID No:46) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COP9 complex subunit 7a" encoded by a nucleic acid that hybridizes to the "COP9 complex subunit 7a" nucleic acid or its complement under low stringency conditions,
- (viii) "COPS3" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPS3" encoded by a nucleic acid that hybridizes to the "COPS3" nucleic acid or its complement under low stringency conditions,
- (ix) "COPS5" (SEQ ID No:48) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPS5" encoded by a

nucleic acid that hybridizes to the "COPS5" nucleic acid or its complement under low stringency conditions,

(x) "COPS6: COP9 subunit 6 (MOV34 homolog, 34 kD)" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPS6: COP9 subunit 6 (MOV34 homolog, 34 kD)" encoded by a nucleic acid that hybridizes to the "COPS6: COP9 subunit 6 (MOV34 homolog, 34 kD)" nucleic acid or its complement under low stringency conditions,

(xi) "COPS7B" (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPS7B" encoded by a nucleic acid that hybridizes to the "COPS7B" nucleic acid or its complement under low stringency conditions,

(xii) "CUL3" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CUL3" encoded by a nucleic acid that hybridizes to the "CUL3" nucleic acid or its complement under low stringency conditions,

(xiii) "Contactin1" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Contactin1" encoded by a nucleic acid that hybridizes to the "Contactin1" nucleic acid or its complement under low stringency conditions,

(xiv) "FLJ12599" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ12599" encoded by a nucleic acid that hybridizes to the "FLJ12599" nucleic acid or its complement under low stringency conditions,

(xv) "Fe65L2" (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L2" encoded by a nucleic acid that hybridizes to the "Fe65L2" nucleic acid or its complement under low stringency conditions,

(xvi) "GPR49" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPR49" encoded by a nucleic acid that hybridizes to the "GPR49" nucleic acid or its complement under low stringency conditions,

(xvii) "GPS1" (SEQ ID No:55) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPS1" encoded by a

- nucleic acid that hybridizes to the "GPS1" nucleic acid or its complement under low stringency conditions,
- (xviii) "KIAA1102 PROTEIN (FRAGMENT)" (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1102 PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xix) "NEDD8" (SEQ ID No:57) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEDD8" encoded by a nucleic acid that hybridizes to the "NEDD8" nucleic acid or its complement under low stringency conditions,
- (xx) "Protocadherin gamma C3" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin gamma C3" encoded by a nucleic acid that hybridizes to the "Protocadherin gamma C3" nucleic acid or its complement under low stringency conditions,
- (xxi) "RBX1" (SEQ ID No:59) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RBX1" encoded by a nucleic acid that hybridizes to the "RBX1" nucleic acid or its complement under low stringency conditions,
- (xxii) "RHOBTB1" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RHOBTB1" encoded by a nucleic acid that hybridizes to the "RHOBTB1" nucleic acid or its complement under low stringency conditions,
- (xxiii) "RHOBTB2" (SEQ ID No:61) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RHOBTB2" encoded by a nucleic acid that hybridizes to the "RHOBTB2" nucleic acid or its complement under low stringency conditions,
- (xxiv) "SIM TO CGI-20" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIM TO CGI-20" encoded by a nucleic acid that hybridizes to the "SIM TO CGI-20" nucleic acid or its complement under low stringency conditions,
- (xxv) "SIMILAR TO POL POLYPROTEIN" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a

variant of "SIMILAR TO POL POLYPROTEIN" encoded by a nucleic acid that hybridizes to the "SIMILAR TO POL POLYPROTEIN" nucleic acid or its complement under low stringency conditions,

(xxvi) "TRIP15" (SEQ ID No:64) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TRIP15" encoded by a nucleic acid that hybridizes to the "TRIP15" nucleic acid or its complement under low stringency conditions,

(xxvii) "TUBGCP3" (SEQ ID No:65) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TUBGCP3" encoded by a nucleic acid that hybridizes to the "TUBGCP3" nucleic acid or its complement under low stringency conditions, and/or(xxviii) "USP11" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "USP11" encoded by a nucleic acid that hybridizes to the "USP11" nucleic acid or its complement under low stringency conditions,as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; cancer such as prostate cancer and breast cancer and skin cancer .

The invention further relates to the following embodiments of the Pilt-complex

1. A protein complex selected from complex (I) and comprising

(a) at least one first protein selected from the group consisting of:

(i) "DLG1" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DLG1" encoded by a nucleic acid that hybridizes to the "DLG1" nucleic acid or its complement under low stringency conditions, and

(ii) "Pilt" (SEQ ID No:72) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pilt" encoded by a nucleic acid that hybridizes to the "Pilt" nucleic acid or its complement under low stringency conditions, and

(b) at least one second protein, which second protein is selected from the group consisting of:

(i) "HYPOTHETICAL PROTEIN (FRAGMENT)" (SEQ ID No:68) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a

variant of "HYPOTHETICAL PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(ii) "HYPOTHETICAL PROTEIN FLJ12599" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ12599" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ12599" nucleic acid or its complement under low stringency conditions,

(iii) "HYPOTHETICAL PROTEIN FLJ35393" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ35393" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ35393" nucleic acid or its complement under low stringency conditions,

(iv) "KIAA1102 (Fragment) " (SEQ ID No:70) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment) " encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment) " nucleic acid or its complement under low stringency conditions,

(v) "KIAA1949 (FRAGMENT)" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1949 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(vi) "STMN3" (SEQ ID No:73) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions, and

(vii) "X11beta" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a

buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

2. The protein complex according to No. 1 wherein the first protein is the protein Pilt (SEQ ID NO. 72), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of 'Pilt' encoded by a nucleic acid that hybridizes to the 'Pilt' under low stringency conditions.
3. The protein complex according to No. 1 selected from complex (I) and comprising the following proteins:
 - (i) "DLG1" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DLG1" encoded by a nucleic acid that hybridizes to the "DLG1" nucleic acid or its complement under low stringency conditions,
 - (ii) "HYPOTHETICAL PROTEIN (FRAGMENT)" (SEQ ID No:68) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
 - (iii) "HYPOTHETICAL PROTEIN FLJ12599" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ12599" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ12599" nucleic acid or its complement under low stringency conditions,
 - (iv) "HYPOTHETICAL PROTEIN FLJ35393" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ35393" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ35393" nucleic acid or its complement under low stringency conditions,
 - (v) "KIAA1102 (Fragment) " (SEQ ID No:70) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment) " encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment) " nucleic acid or its complement under low stringency conditions,

- (vi) "KIAA1949 (FRAGMENT)" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1949 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (vii) "Pilt" (SEQ ID No:72) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pilt" encoded by a nucleic acid that hybridizes to the "Pilt" nucleic acid or its complement under low stringency conditions,
- (viii) "STMN3" (SEQ ID No:73) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "X11beta" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 6 of the following proteins:

- (i) "DLG1" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DLG1" encoded by a nucleic acid that hybridizes to the "DLG1" nucleic acid or its complement under low stringency conditions,
- (ii) "HYPOTHETICAL PROTEIN (FRAGMENT)" (SEQ ID No:68) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (iii) "HYPOTHETICAL PROTEIN FLJ12599" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ12599" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ12599" nucleic acid or its complement under low stringency conditions,

- (iv) "HYPOTHETICAL PROTEIN FLJ35393" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ35393" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ35393" nucleic acid or its complement under low stringency conditions,
- (v) "KIAA1102 (Fragment)" (SEQ ID No:70) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,
- (vi) "KIAA1949 (FRAGMENT)" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1949 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (vii) "Pilt" (SEQ ID No:72) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pilt" encoded by a nucleic acid that hybridizes to the "Pilt" nucleic acid or its complement under low stringency conditions,
- (viii) "STMN3" (SEQ ID No:73) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions,
- (ix) "X11beta" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.

6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.
7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.
8. The complex of any of No. 1 - 7 that is involved in the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).
9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps: expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.
10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.
11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.
12. Component of the Pilt obtainable by a process according to any of No. 9 - 11.

13. Protein of the Pilt selected from

- (i) "HYPOTHETICAL PROTEIN (FRAGMENT)" (SEQ ID No:68) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (ii) "HYPOTHETICAL PROTEIN FLJ12599" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ12599" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ12599" nucleic acid or its complement under low stringency conditions,
- (iii) "HYPOTHETICAL PROTEIN FLJ35393" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ35393" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ35393" nucleic acid or its complement under low stringency conditions,
- (iv) "KIAA1102 (Fragment) " (SEQ ID No:70) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment) " encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment) " nucleic acid or its complement under low stringency conditions, and
- (v) "KIAA1949 (FRAGMENT)" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1949 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

14. Nucleic acid encoding a protein according to No. 13.

15. Construct, preferably a vector construct, comprising (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or
(b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).
16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).
17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.
18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.
19. The kit according to No. 18 for processing a substrate of said complex.
20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative disease such as

Alzheimer's disease; inflammatory conditions such as ulcerative colitis, Crohn's disease and atherosclerosis.

21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.

22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.

23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:

(i) "HYPOTHETICAL PROTEIN (FRAGMENT)" (SEQ ID No:68) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(ii) "HYPOTHETICAL PROTEIN FLJ12599" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ12599" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ12599" nucleic acid or its complement under low stringency conditions,

(iii) "HYPOTHETICAL PROTEIN FLJ35393" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ35393" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ35393" nucleic acid or its complement under low stringency conditions,

(iv) "KIAA1102 (Fragment) " (SEQ ID No:70) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment) " encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment) " nucleic acid or its complement under low stringency conditions, and/or

(v) "KIAA1949 (FRAGMENT)" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949

(FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1949 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative disease such as Alzheimer's disease; inflammatory conditions such as ulcerative colitis, Crohn's disease and atherosclerosis.

25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:

- (i) "HYPOTHETICAL PROTEIN (FRAGMENT)" (SEQ ID No:68) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (ii) "HYPOTHETICAL PROTEIN FLJ12599" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ12599" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ12599" nucleic acid or its complement under low stringency conditions,
- (iii) "HYPOTHETICAL PROTEIN FLJ35393" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ35393" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ35393" nucleic acid or its complement under low stringency conditions,
- (iv) "KIAA1102 (Fragment) " (SEQ ID No:70) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment) " encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment) " nucleic acid or its complement under low stringency conditions, and/or
- (v) "KIAA1949 (FRAGMENT)" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1949

(FRAGMENT)" nucleic acid or its complement under low stringency conditions, comprising the steps of
(a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and
(b) determinig whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of(a) exposing said complex, or a cell or organism containing Pilt to one or more candidate molecules; and

(b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.

28. The method of No. 26, wherein the activity of said complex is determined.

29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.

30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.

31. The method of No. 30, wherein said determining step comprises determining whether

- (i) "DLG1" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DLG1" encoded by a nucleic acid that hybridizes to the "DLG1" nucleic acid or its complement under low stringency conditions, and/or
- (ii) "HYPOTHETICAL PROTEIN (FRAGMENT)" (SEQ ID No:68) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "HYPOTHETICAL PROTEIN FLJ12599" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ12599" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ12599" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "HYPOTHETICAL PROTEIN FLJ35393" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ35393" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ35393" nucleic acid or its complement under low stringency conditions, and/or
- (v) "KIAA1102 (Fragment) " (SEQ ID No:70) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment) " encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment) " nucleic acid or its complement under low stringency conditions, and/or
- (vi) "KIAA1949 (FRAGMENT)" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1949 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "Pilt" (SEQ ID No:72) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pilt" encoded by a nucleic

acid that hybridizes to the "Pilt" nucleic acid or its complement under low stringency conditions, and/or

(viii) "STMN3" (SEQ ID No:73) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions, and/or

(ix) "X11beta" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; inflammatory conditions such as ulcerative colitis, Crohn's disease and atherosclerosis.

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; inflammatory conditions such as ulcerative colitis, Crohn's disease and atherosclerosis.

34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent

on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.
37. The method of No. 35, wherein the activity of said complex is determined.
38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.
39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.
40. The method of No. 39, wherein said determining step comprises determining whether
 - (i) "DLG1" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DLG1" encoded by a nucleic acid that hybridizes to the "DLG1" nucleic acid or its complement under low stringency conditions, and/or
 - (ii) "HYPOTHETICAL PROTEIN (FRAGMENT)" (SEQ ID No:68) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or
 - (iii) "HYPOTHETICAL PROTEIN FLJ12599" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ12599" encoded by a nucleic acid that

hybridizes to the "HYPOTHETICAL PROTEIN FLJ12599" nucleic acid or its complement under low stringency conditions, and/or

(iv) "HYPOTHETICAL PROTEIN FLJ35393" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ35393" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ35393" nucleic acid or its complement under low stringency conditions, and/or

(v) "KIAA1102 (Fragment)" (SEQ ID No:70) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions, and/or

(vi) "KIAA1949 (FRAGMENT)" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1949 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or

(vii) "Pilt" (SEQ ID No:72) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pilt" encoded by a nucleic acid that hybridizes to the "Pilt" nucleic acid or its complement under low stringency conditions, and/or

(viii) "STMN3" (SEQ ID No:73) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions, and/or

(ix) "X11beta" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; inflammatory conditions such as ulcerative colitis, Crohn's disease and arteriosclerosis.

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42 , wherein said disease or disorder involves increased levels of the amount or activity of said complex.

45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins

(i) "DLG1" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DLG1" encoded by a nucleic acid that hybridizes to the "DLG1" nucleic acid or its complement under low stringency conditions,

(ii) "HYPOTHETICAL PROTEIN (FRAGMENT)" (SEQ ID No:68) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

- (iii) "HYPOTHETICAL PROTEIN FLJ12599" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ12599" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ12599" nucleic acid or its complement under low stringency conditions,
- (iv) "HYPOTHETICAL PROTEIN FLJ35393" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ35393" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ35393" nucleic acid or its complement under low stringency conditions,
- (v) "KIAA1102 (Fragment)" (SEQ ID No:70) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,
- (vi) "KIAA1949 (FRAGMENT)" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1949 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (vii) "Pilt" (SEQ ID No:72) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pilt" encoded by a nucleic acid that hybridizes to the "Pilt" nucleic acid or its complement under low stringency conditions,
- (viii) "STMN3" (SEQ ID No:73) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions, and/or(ix) "X11beta" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions,as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; inflammatory conditions such as ulcerative colitis, Crohn's disease and atherosclerosis.

The invention further relates to the following embodiments of the Neurotrypsin-complex

1. A protein complex selected from complex (I) and comprising

(a) at least one first protein selected from the group consisting of:

(i) "Neurotrypsin" (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions, and

(b) at least one second protein, which second protein is selected from the group consisting of:

(i) "ADAMTS1" (SEQ ID No:75) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS1" encoded by a nucleic acid that hybridizes to the "ADAMTS1" nucleic acid or its complement under low stringency conditions,

(ii) "ADAMTS19" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS19" encoded by a nucleic acid that hybridizes to the "ADAMTS19" nucleic acid or its complement under low stringency conditions,

(iii) "ADAMTS7" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS7" encoded by a nucleic acid that hybridizes to the "ADAMTS7" nucleic acid or its complement under low stringency conditions,

(iv) "CHRNA5" (SEQ ID No:78) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CHRNA5" encoded by a nucleic acid that hybridizes to the "CHRNA5" nucleic acid or its complement under low stringency conditions,

(v) "CRTAP" (SEQ ID No:79) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CRTAP" encoded by a nucleic acid that hybridizes to the "CRTAP" nucleic acid or its complement under low stringency conditions,

(vi) "CU70_HUMAN" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CU70_HUMAN" encoded by a nucleic acid that hybridizes to the "CU70_HUMAN" nucleic acid or its complement under low stringency conditions,

- (vii) "DECR1" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DECR1" encoded by a nucleic acid that hybridizes to the "DECR1" nucleic acid or its complement under low stringency conditions,
- (viii) "DNAJC3" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNAJC3" encoded by a nucleic acid that hybridizes to the "DNAJC3" nucleic acid or its complement under low stringency conditions,
- (ix) "ERP70" (SEQ ID No:83) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ERP70" encoded by a nucleic acid that hybridizes to the "ERP70" nucleic acid or its complement under low stringency conditions,
- (x) "GBTS1" (SEQ ID No:84) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GBTS1" encoded by a nucleic acid that hybridizes to the "GBTS1" nucleic acid or its complement under low stringency conditions,
- (xi) "GRCB" (SEQ ID No:85) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GRCB" encoded by a nucleic acid that hybridizes to the "GRCB" nucleic acid or its complement under low stringency conditions,
- (xii) "Hypothetical protein KIAA1402 (Fragment)" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA1402 (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA1402 (Fragment)" nucleic acid or its complement under low stringency conditions,
- (xiii) "LAMB1" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LAMB1" encoded by a nucleic acid that hybridizes to the "LAMB1" nucleic acid or its complement under low stringency conditions,
- (xiv) "Laminin, gamma 1 " (SEQ ID No:88) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Laminin, gamma 1 " encoded by a nucleic acid that hybridizes to the "Laminin, gamma 1 " nucleic acid or its complement under low stringency conditions,

- (xv) "MT-ACT48" (SEQ ID No:89) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MT-ACT48" encoded by a nucleic acid that hybridizes to the "MT-ACT48" nucleic acid or its complement under low stringency conditions,
- (xvi) "NOTCH4-like protein (Hypothetical protein)" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NOTCH4-like protein (Hypothetical protein)" encoded by a nucleic acid that hybridizes to the "NOTCH4-like protein (Hypothetical protein)" nucleic acid or its complement under low stringency conditions,
- (xvii) "PCDH16" (SEQ ID No:92) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDH16" encoded by a nucleic acid that hybridizes to the "PCDH16" nucleic acid or its complement under low stringency conditions,
- (xviii) "PLOD" (SEQ ID No:93) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PLOD" encoded by a nucleic acid that hybridizes to the "PLOD" nucleic acid or its complement under low stringency conditions,
- (xix) "PLOD3" (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PLOD3" encoded by a nucleic acid that hybridizes to the "PLOD3" nucleic acid or its complement under low stringency conditions,
- (xx) "PUTATIVE DNA POLYMERASE DELTA P38 SUBUNIT" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PUTATIVE DNA POLYMERASE DELTA P38 SUBUNIT" encoded by a nucleic acid that hybridizes to the "PUTATIVE DNA POLYMERASE DELTA P38 SUBUNIT" nucleic acid or its complement under low stringency conditions,
- (xxi) "RAB39, MEMBER RAS ONCOGENE FAMILY" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB39, MEMBER RAS ONCOGENE FAMILY" encoded by a nucleic acid that hybridizes to the "RAB39, MEMBER RAS ONCOGENE FAMILY" nucleic acid or its complement under low stringency conditions,
- (xxii) "Reelin" (SEQ ID No:97) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Reelin" encoded by a

nucleic acid that hybridizes to the "Reelin" nucleic acid or its complement under low stringency conditions,

(xxiii) "SC65" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SC65" encoded by a nucleic acid that hybridizes to the "SC65" nucleic acid or its complement under low stringency conditions,

(xxiv) "Similar to RIKEN cDNA 1300010F03 gene" (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to RIKEN cDNA 1300010F03 gene" encoded by a nucleic acid that hybridizes to the "Similar to RIKEN cDNA 1300010F03 gene" nucleic acid or its complement under low stringency conditions,

(xxv) "Similar to hydroxysteroid 17-beta dehydrogenase 11" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to hydroxysteroid 17-beta dehydrogenase 11" encoded by a nucleic acid that hybridizes to the "Similar to hydroxysteroid 17-beta dehydrogenase 11" nucleic acid or its complement under low stringency conditions,

(xxvi) "Similar to hypothetical protein FLJ22329" (SEQ ID No:101) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to hypothetical protein FLJ22329" encoded by a nucleic acid that hybridizes to the "Similar to hypothetical protein FLJ22329" nucleic acid or its complement under low stringency conditions,

(xxvii) "UGCGL2" (SEQ ID No:102) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "UGCGL2" encoded by a nucleic acid that hybridizes to the "UGCGL2" nucleic acid or its complement under low stringency conditions,

(xxviii) "hyou1: hypoxia up-regulated 1" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hyou1: hypoxia up-regulated 1" encoded by a nucleic acid that hybridizes to the "hyou1: hypoxia up-regulated 1" nucleic acid or its complement under low stringency conditions, and

(xxix) "q8wvi0" (SEQ ID No:104) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "q8wvi0" encoded by a nucleic acid that hybridizes to the "q8wvi0" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said

nucleic acid that hybridizes to the "CRTAP" nucleic acid or its complement under low stringency conditions,

(vi) "CU70_HUMAN" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CU70_HUMAN" encoded by a nucleic acid that hybridizes to the "CU70_HUMAN" nucleic acid or its complement under low stringency conditions,

(vii) "DECR1" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DECR1" encoded by a nucleic acid that hybridizes to the "DECR1" nucleic acid or its complement under low stringency conditions,

(viii) "DNAJC3" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNAJC3" encoded by a nucleic acid that hybridizes to the "DNAJC3" nucleic acid or its complement under low stringency conditions,

(ix) "ERP70" (SEQ ID No:83) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ERP70" encoded by a nucleic acid that hybridizes to the "ERP70" nucleic acid or its complement under low stringency conditions,

(x) "GBTS1" (SEQ ID No:84) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GBTS1" encoded by a nucleic acid that hybridizes to the "GBTS1" nucleic acid or its complement under low stringency conditions,

(xi) "GRCB" (SEQ ID No:85) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GRCB" encoded by a nucleic acid that hybridizes to the "GRCB" nucleic acid or its complement under low stringency conditions,

(xii) "Hypothetical protein KIAA1402 (Fragment)" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA1402 (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA1402 (Fragment)" nucleic acid or its complement under low stringency conditions,

(xiii) "LAMB1" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LAMB1" encoded by a

second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

2. The protein complex according to No. 1 wherein the first protein is the protein Neurotrypsin (SEQ ID NO. 91), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of 'Neurotrypsin' encoded by a nucleic acid that hybridizes to the 'Neurotrypsin' under low stringency conditions.

3. The protein complex according to No. 1 selected from complex (I) and comprising the following proteins:

- (i) "ADAMTS1" (SEQ ID No:75) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS1" encoded by a nucleic acid that hybridizes to the "ADAMTS1" nucleic acid or its complement under low stringency conditions,
- (ii) "ADAMTS19" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS19" encoded by a nucleic acid that hybridizes to the "ADAMTS19" nucleic acid or its complement under low stringency conditions,
- (iii) "ADAMTS7" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS7" encoded by a nucleic acid that hybridizes to the "ADAMTS7" nucleic acid or its complement under low stringency conditions,
- (iv) "CHRNA5" (SEQ ID No:78) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CHRNA5" encoded by a nucleic acid that hybridizes to the "CHRNA5" nucleic acid or its complement under low stringency conditions,
- (v) "CRTAP" (SEQ ID No:79) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CRTAP" encoded by a

nucleic acid that hybridizes to the "LAMB1" nucleic acid or its complement under low stringency conditions,

(xiv) "Laminin, gamma 1 " (SEQ ID No:88) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Laminin, gamma 1 " encoded by a nucleic acid that hybridizes to the "Laminin, gamma 1 " nucleic acid or its complement under low stringency conditions,

(xv) "MT-ACT48" (SEQ ID No:89) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MT-ACT48" encoded by a nucleic acid that hybridizes to the "MT-ACT48" nucleic acid or its complement under low stringency conditions,

(xvi) "NOTCH4-like protein (Hypothetical protein)" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NOTCH4-like protein (Hypothetical protein)" encoded by a nucleic acid that hybridizes to the "NOTCH4-like protein (Hypothetical protein)" nucleic acid or its complement under low stringency conditions,

(xvii) "Neurotrypsin" (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,

(xviii) "PCDH16" (SEQ ID No:92) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDH16" encoded by a nucleic acid that hybridizes to the "PCDH16" nucleic acid or its complement under low stringency conditions,

(xix) "PLOD" (SEQ ID No:93) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PLOD" encoded by a nucleic acid that hybridizes to the "PLOD" nucleic acid or its complement under low stringency conditions,

(xx) "PLOD3" (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PLOD3" encoded by a nucleic acid that hybridizes to the "PLOD3" nucleic acid or its complement under low stringency conditions,

(xi) "PUTATIVE DNA POLYMERASE DELTA P38 SUBUNIT" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PUTATIVE DNA POLYMERASE DELTA P38

SUBUNIT" encoded by a nucleic acid that hybridizes to the "PUTATIVE DNA POLYMERASE DELTA P38 SUBUNIT" nucleic acid or its complement under low stringency conditions,

(xxii) "RAB39, MEMBER RAS ONCOGENE FAMILY" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB39, MEMBER RAS ONCOGENE FAMILY" encoded by a nucleic acid that hybridizes to the "RAB39, MEMBER RAS ONCOGENE FAMILY" nucleic acid or its complement under low stringency conditions,

(xxiii) "Reelin" (SEQ ID No:97) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Reelin" encoded by a nucleic acid that hybridizes to the "Reelin" nucleic acid or its complement under low stringency conditions,

(xxiv) "SC65" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SC65" encoded by a nucleic acid that hybridizes to the "SC65" nucleic acid or its complement under low stringency conditions,

(xxv) "Similar to RIKEN cDNA 1300010F03 gene" (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to RIKEN cDNA 1300010F03 gene" encoded by a nucleic acid that hybridizes to the "Similar to RIKEN cDNA 1300010F03 gene" nucleic acid or its complement under low stringency conditions,

(xxvi) "Similar to hydroxysteroid 17-beta dehydrogenase 11" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to hydroxysteroid 17-beta dehydrogenase 11" encoded by a nucleic acid that hybridizes to the "Similar to hydroxysteroid 17-beta dehydrogenase 11" nucleic acid or its complement under low stringency conditions,

(xxvii) "Similar to hypothetical protein FLJ22329" (SEQ ID No:101) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to hypothetical protein FLJ22329" encoded by a nucleic acid that hybridizes to the "Similar to hypothetical protein FLJ22329" nucleic acid or its complement under low stringency conditions,

(xxviii) "UGCGL2" (SEQ ID No:102) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "UGCGL2"

encoded by a nucleic acid that hybridizes to the "UGCGL2" nucleic acid or its complement under low stringency conditions,

(xxix) "hyou1: hypoxia up-regulated 1" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hyou1: hypoxia up-regulated 1" encoded by a nucleic acid that hybridizes to the "hyou1: hypoxia up-regulated 1" nucleic acid or its complement under low stringency conditions, and/or

(xxx) "q8wwi0" (SEQ ID No:104) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "q8wwi0" encoded by a nucleic acid that hybridizes to the "q8wwi0" nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 28 of the following proteins:

(i) "ADAMTS1" (SEQ ID No:75) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS1" encoded by a nucleic acid that hybridizes to the "ADAMTS1" nucleic acid or its complement under low stringency conditions,

(ii) "ADAMTS19" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS19" encoded by a nucleic acid that hybridizes to the "ADAMTS19" nucleic acid or its complement under low stringency conditions,

(iii) "ADAMTS7" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS7" encoded by a nucleic acid that hybridizes to the "ADAMTS7" nucleic acid or its complement under low stringency conditions,

(iv) "CHRNA5" (SEQ ID No:78) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CHRNA5" encoded by a nucleic acid that hybridizes to the "CHRNA5" nucleic acid or its complement under low stringency conditions,

(v) "CRTAP" (SEQ ID No:79) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CRTAP" encoded by a nucleic acid that hybridizes to the "CRTAP" nucleic acid or its complement under low stringency conditions,

- (vi) "CU70_HUMAN" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CU70_HUMAN" encoded by a nucleic acid that hybridizes to the "CU70_HUMAN" nucleic acid or its complement under low stringency conditions,
- (vii) "DECR1" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DECR1" encoded by a nucleic acid that hybridizes to the "DECR1" nucleic acid or its complement under low stringency conditions,
- (viii) "DNAJC3" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNAJC3" encoded by a nucleic acid that hybridizes to the "DNAJC3" nucleic acid or its complement under low stringency conditions,
- (ix) "ERP70" (SEQ ID No:83) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ERP70" encoded by a nucleic acid that hybridizes to the "ERP70" nucleic acid or its complement under low stringency conditions,
- (x) "GBTS1" (SEQ ID No:84) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GBTS1" encoded by a nucleic acid that hybridizes to the "GBTS1" nucleic acid or its complement under low stringency conditions,
- (xi) "GRCB" (SEQ ID No:85) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GRCB" encoded by a nucleic acid that hybridizes to the "GRCB" nucleic acid or its complement under low stringency conditions,
- (xii) "Hypothetical protein KIAA1402 (Fragment)" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA1402 (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA1402 (Fragment)" nucleic acid or its complement under low stringency conditions,
- (xiii) "LAMB1" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LAMB1" encoded by a nucleic acid that hybridizes to the "LAMB1" nucleic acid or its complement under low stringency conditions,

- (xiv) "Laminin, gamma 1 " (SEQ ID No:88) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Laminin, gamma 1 " encoded by a nucleic acid that hybridizes to the "Laminin, gamma 1 " nucleic acid or its complement under low stringency conditions,
- (xv) "MT-ACT48" (SEQ ID No:89) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MT-ACT48" encoded by a nucleic acid that hybridizes to the "MT-ACT48" nucleic acid or its complement under low stringency conditions,
- (xvi) "NOTCH4-like protein (Hypothetical protein)" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NOTCH4-like protein (Hypothetical protein)" encoded by a nucleic acid that hybridizes to the "NOTCH4-like protein (Hypothetical protein)" nucleic acid or its complement under low stringency conditions,
- (xvii) "Neurotrypsin" (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,
- (xviii) "PCDH16" (SEQ ID No:92) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDH16" encoded by a nucleic acid that hybridizes to the "PCDH16" nucleic acid or its complement under low stringency conditions,
- (xix) "PLOD" (SEQ ID No:93) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PLOD" encoded by a nucleic acid that hybridizes to the "PLOD" nucleic acid or its complement under low stringency conditions,
- (xx) "PLOD3" (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PLOD3" encoded by a nucleic acid that hybridizes to the "PLOD3" nucleic acid or its complement under low stringency conditions,
- (xxi) "PUTATIVE DNA POLYMERASE DELTA P38 SUBUNIT" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PUTATIVE DNA POLYMERASE DELTA P38 SUBUNIT" encoded by a nucleic acid that hybridizes to the "PUTATIVE DNA

POLYMERASE DELTA P38 SUBUNIT" nucleic acid or its complement under low stringency conditions,

(xxii) "RAB39, MEMBER RAS ONCOGENE FAMILY" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB39, MEMBER RAS ONCOGENE FAMILY" encoded by a nucleic acid that hybridizes to the "RAB39, MEMBER RAS ONCOGENE FAMILY" nucleic acid or its complement under low stringency conditions,

(xxiii) "Reelin" (SEQ ID No:97) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Reelin" encoded by a nucleic acid that hybridizes to the "Reelin" nucleic acid or its complement under low stringency conditions,

(xxiv) "SC65" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SC65" encoded by a nucleic acid that hybridizes to the "SC65" nucleic acid or its complement under low stringency conditions,

(xxv) "Similar to RIKEN cDNA 1300010F03 gene" (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to RIKEN cDNA 1300010F03 gene" encoded by a nucleic acid that hybridizes to the "Similar to RIKEN cDNA 1300010F03 gene" nucleic acid or its complement under low stringency conditions,

(xxvi) "Similar to hydroxysteroid 17-beta dehydrogenase 11" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to hydroxysteroid 17-beta dehydrogenase 11" encoded by a nucleic acid that hybridizes to the "Similar to hydroxysteroid 17-beta dehydrogenase 11" nucleic acid or its complement under low stringency conditions,

(xxvii) "Similar to hypothetical protein FLJ22329" (SEQ ID No:101) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to hypothetical protein FLJ22329" encoded by a nucleic acid that hybridizes to the "Similar to hypothetical protein FLJ22329" nucleic acid or its complement under low stringency conditions,

(xxviii) "UGCGL2" (SEQ ID No:102) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "UGCGL2" encoded by a nucleic acid that hybridizes to the "UGCGL2" nucleic acid or its complement under low stringency conditions,

(xxix) "hyou1: hypoxia up-regulated 1" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hyou1: hypoxia up-regulated 1" encoded by a nucleic acid that hybridizes to the "hyou1: hypoxia up-regulated 1" nucleic acid or its complement under low stringency conditions, (xxx) "q8wwi0" (SEQ ID No:104) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "q8wwi0" encoded by a nucleic acid that hybridizes to the "q8wwi0" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.
6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.
7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.
8. The complex of any of No. 1 - 7 that is involved in the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).

9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps: expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.

10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.

11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.

12. Component of the Neurotrypsin obtainable by a process according to any of No. 9 - 11.

13. Protein of the Neurotrypsin selected from

- (i) "ADAMTS19" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS19" encoded by a nucleic acid that hybridizes to the "ADAMTS19" nucleic acid or its complement under low stringency conditions,
- (ii) "ADAMTS7" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS7" encoded by a nucleic acid that hybridizes to the "ADAMTS7" nucleic acid or its complement under low stringency conditions,
- (iii) "CRTAP" (SEQ ID No:79) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CRTAP" encoded by a nucleic acid that hybridizes to the "CRTAP" nucleic acid or its complement under low stringency conditions,
- (iv) "CU70_HUMAN" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CU70_HUMAN" encoded by a nucleic acid that hybridizes to the "CU70_HUMAN" nucleic acid or its complement under low stringency conditions,

- (v) "GBTS1" (SEQ ID No:84) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GBTS1" encoded by a nucleic acid that hybridizes to the "GBTS1" nucleic acid or its complement under low stringency conditions,
- (vi) "GRCB" (SEQ ID No:85) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GRCB" encoded by a nucleic acid that hybridizes to the "GRCB" nucleic acid or its complement under low stringency conditions,
- (vii) "Hypothetical protein KIAA1402 (Fragment)" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA1402 (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA1402 (Fragment)" nucleic acid or its complement under low stringency conditions,
- (viii) "MT-ACT48" (SEQ ID No:89) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MT-ACT48" encoded by a nucleic acid that hybridizes to the "MT-ACT48" nucleic acid or its complement under low stringency conditions,
- (ix) "PCDH16" (SEQ ID No:92) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDH16" encoded by a nucleic acid that hybridizes to the "PCDH16" nucleic acid or its complement under low stringency conditions,
- (x) "PUTATIVE DNA POLYMERASE DELTA P38 SUBUNIT" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PUTATIVE DNA POLYMERASE DELTA P38 SUBUNIT" encoded by a nucleic acid that hybridizes to the "PUTATIVE DNA POLYMERASE DELTA P38 SUBUNIT" nucleic acid or its complement under low stringency conditions,
- (xi) "RAB39, MEMBER RAS ONCOGENE FAMILY" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB39, MEMBER RAS ONCOGENE FAMILY" encoded by a nucleic acid that hybridizes to the "RAB39, MEMBER RAS ONCOGENE FAMILY" nucleic acid or its complement under low stringency conditions,
- (xii) "SC65" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SC65" encoded by a

nucleic acid that hybridizes to the "SC65" nucleic acid or its complement under low stringency conditions,

(xiii) "Similar to RIKEN cDNA 1300010F03 gene" (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to RIKEN cDNA 1300010F03 gene" encoded by a nucleic acid that hybridizes to the "Similar to RIKEN cDNA 1300010F03 gene" nucleic acid or its complement under low stringency conditions,

(xiv) "Similar to hydroxysteroid 17-beta dehydrogenase 11" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to hydroxysteroid 17-beta dehydrogenase 11" encoded by a nucleic acid that hybridizes to the "Similar to hydroxysteroid 17-beta dehydrogenase 11" nucleic acid or its complement under low stringency conditions,

(xv) "Similar to hypothetical protein FLJ22329" (SEQ ID No:101) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to hypothetical protein FLJ22329" encoded by a nucleic acid that hybridizes to the "Similar to hypothetical protein FLJ22329" nucleic acid or its complement under low stringency conditions, and

(xvi) "q8wwi0" (SEQ ID No:104) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "q8wwi0" encoded by a nucleic acid that hybridizes to the "q8wwi0" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

14. Nucleic acid encoding a protein according to No. 13.

15. Construct, preferably a vector construct, comprising (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or

(b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).

16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).

17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.

18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.

19. The kit according to No. 18 for processing a substrate of said complex.

20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.

22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.

23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:

- (i) "ADAMTS19" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS19" encoded by a nucleic acid that hybridizes to the "ADAMTS19" nucleic acid or its complement under low stringency conditions,
- (ii) "ADAMTS7" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS7" encoded by a nucleic acid that hybridizes to the "ADAMTS7" nucleic acid or its complement under low stringency conditions,
- (iii) "CRTAP" (SEQ ID No:79) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CRTAP" encoded by a nucleic acid that hybridizes to the "CRTAP" nucleic acid or its complement under low stringency conditions,
- (iv) "CU70_HUMAN" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CU70_HUMAN" encoded by a nucleic acid that hybridizes to the "CU70_HUMAN" nucleic acid or its complement under low stringency conditions,
- (v) "GBTS1" (SEQ ID No:84) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GBTS1" encoded by a nucleic acid that hybridizes to the "GBTS1" nucleic acid or its complement under low stringency conditions,
- (vi) "GRCB" (SEQ ID No:85) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GRCB" encoded by a nucleic acid that hybridizes to the "GRCB" nucleic acid or its complement under low stringency conditions,

- (vii) "Hypothetical protein KIAA1402 (Fragment)" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA1402 (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA1402 (Fragment)" nucleic acid or its complement under low stringency conditions,
- (viii) "MT-ACT48" (SEQ ID No:89) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MT-ACT48" encoded by a nucleic acid that hybridizes to the "MT-ACT48" nucleic acid or its complement under low stringency conditions,
- (ix) "PCDH16" (SEQ ID No:92) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDH16" encoded by a nucleic acid that hybridizes to the "PCDH16" nucleic acid or its complement under low stringency conditions,
- (x) "PUTATIVE DNA POLYMERASE DELTA P38 SUBUNIT" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PUTATIVE DNA POLYMERASE DELTA P38 SUBUNIT" encoded by a nucleic acid that hybridizes to the "PUTATIVE DNA POLYMERASE DELTA P38 SUBUNIT" nucleic acid or its complement under low stringency conditions,
- (xi) "RAB39, MEMBER RAS ONCOGENE FAMILY" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB39, MEMBER RAS ONCOGENE FAMILY" encoded by a nucleic acid that hybridizes to the "RAB39, MEMBER RAS ONCOGENE FAMILY" nucleic acid or its complement under low stringency conditions,
- (xii) "SC65" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SC65" encoded by a nucleic acid that hybridizes to the "SC65" nucleic acid or its complement under low stringency conditions,
- (xiii) "Similar to RIKEN cDNA 1300010F03 gene" (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to RIKEN cDNA 1300010F03 gene" encoded by a nucleic acid that hybridizes to the "Similar to RIKEN cDNA 1300010F03 gene" nucleic acid or its complement under low stringency conditions,

- (xiv) "Similar to hydroxysteroid 17-beta dehydrogenase 11" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to hydroxysteroid 17-beta dehydrogenase 11" encoded by a nucleic acid that hybridizes to the "Similar to hydroxysteroid 17-beta dehydrogenase 11" nucleic acid or its complement under low stringency conditions,
- (xv) "Similar to hypothetical protein FLJ22329" (SEQ ID No:101) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to hypothetical protein FLJ22329" encoded by a nucleic acid that hybridizes to the "Similar to hypothetical protein FLJ22329" nucleic acid or its complement under low stringency conditions, and/or
- (xvi) "q8wvi0" (SEQ ID No:104) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "q8wvi0" encoded by a nucleic acid that hybridizes to the "q8wvi0" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:

- (i) "ADAMTS19" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS19" encoded by a nucleic acid that hybridizes to the "ADAMTS19" nucleic acid or its complement under low stringency conditions,
- (ii) "ADAMTS7" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS7" encoded by a nucleic acid that hybridizes to the "ADAMTS7" nucleic acid or its complement under low stringency conditions,
- (iii) "CRTAP" (SEQ ID No:79) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CRTAP" encoded by a

nucleic acid that hybridizes to the "CRTAP" nucleic acid or its complement under low stringency conditions,

(iv) "CU70_HUMAN" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CU70_HUMAN" encoded by a nucleic acid that hybridizes to the "CU70_HUMAN" nucleic acid or its complement under low stringency conditions,

(v) "GBTS1" (SEQ ID No:84) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GBTS1" encoded by a nucleic acid that hybridizes to the "GBTS1" nucleic acid or its complement under low stringency conditions,

(vi) "GRCB" (SEQ ID No:85) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GRCB" encoded by a nucleic acid that hybridizes to the "GRCB" nucleic acid or its complement under low stringency conditions,

(vii) "Hypothetical protein KIAA1402 (Fragment)" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA1402 (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA1402 (Fragment)" nucleic acid or its complement under low stringency conditions,

(viii) "MT-ACT48" (SEQ ID No:89) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MT-ACT48" encoded by a nucleic acid that hybridizes to the "MT-ACT48" nucleic acid or its complement under low stringency conditions,

(ix) "PCDH16" (SEQ ID No:92) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDH16" encoded by a nucleic acid that hybridizes to the "PCDH16" nucleic acid or its complement under low stringency conditions,

(x) "PUTATIVE DNA POLYMERASE DELTA P38 SUBUNIT" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PUTATIVE DNA POLYMERASE DELTA P38 SUBUNIT" encoded by a nucleic acid that hybridizes to the "PUTATIVE DNA POLYMERASE DELTA P38 SUBUNIT" nucleic acid or its complement under low stringency conditions,

- (xi) "RAB39, MEMBER RAS ONCOGENE FAMILY" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB39, MEMBER RAS ONCOGENE FAMILY" encoded by a nucleic acid that hybridizes to the "RAB39, MEMBER RAS ONCOGENE FAMILY" nucleic acid or its complement under low stringency conditions,
- (xii) "SC65" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SC65" encoded by a nucleic acid that hybridizes to the "SC65" nucleic acid or its complement under low stringency conditions,
- (xiii) "Similar to RIKEN cDNA 1300010F03 gene" (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to RIKEN cDNA 1300010F03 gene" encoded by a nucleic acid that hybridizes to the "Similar to RIKEN cDNA 1300010F03 gene" nucleic acid or its complement under low stringency conditions,
- (xiv) "Similar to hydroxysteroid 17-beta dehydrogenase 11" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to hydroxysteroid 17-beta dehydrogenase 11" encoded by a nucleic acid that hybridizes to the "Similar to hydroxysteroid 17-beta dehydrogenase 11" nucleic acid or its complement under low stringency conditions,
- (xv) "Similar to hypothetical protein FLJ22329" (SEQ ID No:101) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to hypothetical protein FLJ22329" encoded by a nucleic acid that hybridizes to the "Similar to hypothetical protein FLJ22329" nucleic acid or its complement under low stringency conditions, and/or
- (xvi) "q8wvi0" (SEQ ID No:104) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "q8wvi0" encoded by a nucleic acid that hybridizes to the "q8wvi0" nucleic acid or its complement under low stringency conditions, comprising the steps of
 - (a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and
 - (b) determining whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8

comprising the steps of(a) exposing said complex, or a cell or organism containing Neurotrypsin to one or more candidate molecules; and

(b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.

28. The method of No. 26, wherein the activity of said complex is determined.

29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.

30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.

31. The method of No. 30, wherein said determining step comprises determining whether (i) "ADAMTS1" (SEQ ID No:75) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS1" encoded by a nucleic acid that hybridizes to the "ADAMTS1" nucleic acid or its complement under low stringency conditions, and/or

- (ii) "ADAMTS19" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS19" encoded by a nucleic acid that hybridizes to the "ADAMTS19" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "ADAMTS7" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS7" encoded by a nucleic acid that hybridizes to the "ADAMTS7" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "CHRNA5" (SEQ ID No:78) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CHRNA5" encoded by a nucleic acid that hybridizes to the "CHRNA5" nucleic acid or its complement under low stringency conditions, and/or
- (v) "CRTAP" (SEQ ID No:79) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CRTAP" encoded by a nucleic acid that hybridizes to the "CRTAP" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "CU70_HUMAN" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CU70_HUMAN" encoded by a nucleic acid that hybridizes to the "CU70_HUMAN" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "DECR1" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DECR1" encoded by a nucleic acid that hybridizes to the "DECR1" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "DNAJC3" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNAJC3" encoded by a nucleic acid that hybridizes to the "DNAJC3" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "ERP70" (SEQ ID No:83) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ERP70" encoded by a nucleic acid that hybridizes to the "ERP70" nucleic acid or its complement under low stringency conditions, and/or
- (x) "GBTS1" (SEQ ID No:84) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GBTS1" encoded by a

nucleic acid that hybridizes to the "GBTS1" nucleic acid or its complement under low stringency conditions, and/or

(xi) "GRCB" (SEQ ID No:85) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GRCB" encoded by a nucleic acid that hybridizes to the "GRCB" nucleic acid or its complement under low stringency conditions, and/or

(xii) "Hypothetical protein KIAA1402 (Fragment)" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA1402 (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA1402 (Fragment)" nucleic acid or its complement under low stringency conditions, and/or

(xiii) "LAMB1" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LAMB1" encoded by a nucleic acid that hybridizes to the "LAMB1" nucleic acid or its complement under low stringency conditions, and/or

(xiv) "Laminin, gamma 1 " (SEQ ID No:88) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Laminin, gamma 1 " encoded by a nucleic acid that hybridizes to the "Laminin, gamma 1 " nucleic acid or its complement under low stringency conditions, and/or

(xv) "MT-ACT48" (SEQ ID No:89) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MT-ACT48" encoded by a nucleic acid that hybridizes to the "MT-ACT48" nucleic acid or its complement under low stringency conditions, and/or

(xvi) "NOTCH4-like protein (Hypothetical protein)" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NOTCH4-like protein (Hypothetical protein)" encoded by a nucleic acid that hybridizes to the "NOTCH4-like protein (Hypothetical protein)" nucleic acid or its complement under low stringency conditions, and/or

(xvii) "Neurotrypsin" (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions, and/or

(xviii) "PCDH16" (SEQ ID No:92) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDH16"

encoded by a nucleic acid that hybridizes to the "PCDH16" nucleic acid or its complement under low stringency conditions, and/or

(xix) "PLOD" (SEQ ID No:93) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PLOD" encoded by a nucleic acid that hybridizes to the "PLOD" nucleic acid or its complement under low stringency conditions, and/or

(xx) "PLOD3" (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PLOD3" encoded by a nucleic acid that hybridizes to the "PLOD3" nucleic acid or its complement under low stringency conditions, and/or

(xxi) "PUTATIVE DNA POLYMERASE DELTA P38 SUBUNIT" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PUTATIVE DNA POLYMERASE DELTA P38 SUBUNIT" encoded by a nucleic acid that hybridizes to the "PUTATIVE DNA POLYMERASE DELTA P38 SUBUNIT" nucleic acid or its complement under low stringency conditions, and/or

(xxii) "RAB39, MEMBER RAS ONCOGENE FAMILY" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB39, MEMBER RAS ONCOGENE FAMILY" encoded by a nucleic acid that hybridizes to the "RAB39, MEMBER RAS ONCOGENE FAMILY" nucleic acid or its complement under low stringency conditions, and/or

(xxiii) "Reelin" (SEQ ID No:97) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Reelin" encoded by a nucleic acid that hybridizes to the "Reelin" nucleic acid or its complement under low stringency conditions, and/or

(xxiv) "SC65" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SC65" encoded by a nucleic acid that hybridizes to the "SC65" nucleic acid or its complement under low stringency conditions, and/or

(xxv) "Similar to RIKEN cDNA 1300010F03 gene" (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to RIKEN cDNA 1300010F03 gene" encoded by a nucleic acid that hybridizes to the "Similar to RIKEN cDNA 1300010F03 gene" nucleic acid or its complement under low stringency conditions, and/or

- (xxvi) "Similar to hydroxysteroid 17-beta dehydrogenase 11" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to hydroxysteroid 17-beta dehydrogenase 11" encoded by a nucleic acid that hybridizes to the "Similar to hydroxysteroid 17-beta dehydrogenase 11" nucleic acid or its complement under low stringency conditions, and/or
- (xxvii) "Similar to hypothetical protein FLJ22329" (SEQ ID No:101) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to hypothetical protein FLJ22329" encoded by a nucleic acid that hybridizes to the "Similar to hypothetical protein FLJ22329" nucleic acid or its complement under low stringency conditions, and/or
- (xxviii) "UGCGL2" (SEQ ID No:102) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "UGCGL2" encoded by a nucleic acid that hybridizes to the "UGCGL2" nucleic acid or its complement under low stringency conditions, and/or
- (xxix) "hyou1: hypoxia up-regulated 1" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hyou1: hypoxia up-regulated 1" encoded by a nucleic acid that hybridizes to the "hyou1: hypoxia up-regulated 1" nucleic acid or its complement under low stringency conditions, and/or
- (xxx) "q8wvi0" (SEQ ID No:104) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "q8wvi0" encoded by a nucleic acid that hybridizes to the "q8wvi0" nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.

37. The method of No. 35, wherein the activity of said complex is determined.

38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

40. The method of No. 39, wherein said determining step comprises determining whether

- (i) "ADAMTS1" (SEQ ID No:75) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS1" encoded by a nucleic acid that hybridizes to the "ADAMTS1" nucleic acid or its complement under low stringency conditions, and/or
- (ii) "ADAMTS19" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS19" encoded by a nucleic acid that hybridizes to the "ADAMTS19" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "ADAMTS7" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS7" encoded by a nucleic acid that hybridizes to the "ADAMTS7" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "CHRNA5" (SEQ ID No:78) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CHRNA5" encoded by a nucleic acid that hybridizes to the "CHRNA5" nucleic acid or its complement under low stringency conditions, and/or
- (v) "CRTAP" (SEQ ID No:79) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CRTAP" encoded by a nucleic acid that hybridizes to the "CRTAP" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "CU70_HUMAN" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CU70_HUMAN" encoded by a nucleic acid that hybridizes to the "CU70_HUMAN" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "DECR1" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DECR1" encoded by a nucleic acid that hybridizes to the "DECR1" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "DNAJC3" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNAJC3" encoded by a nucleic acid that hybridizes to the "DNAJC3" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "ERP70" (SEQ ID No:83) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ERP70" encoded by a

nucleic acid that hybridizes to the "ERP70" nucleic acid or its complement under low stringency conditions, and/or

(x) "GBTS1" (SEQ ID No:84) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GBTS1" encoded by a nucleic acid that hybridizes to the "GBTS1" nucleic acid or its complement under low stringency conditions, and/or

(xi) "GRCB" (SEQ ID No:85) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GRCB" encoded by a nucleic acid that hybridizes to the "GRCB" nucleic acid or its complement under low stringency conditions, and/or

(xii) "Hypothetical protein KIAA1402 (Fragment)" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA1402 (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA1402 (Fragment)" nucleic acid or its complement under low stringency conditions, and/or

(xiii) "LAMB1" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LAMB1" encoded by a nucleic acid that hybridizes to the "LAMB1" nucleic acid or its complement under low stringency conditions, and/or

(xiv) "Laminin, gamma 1 " (SEQ ID No:88) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Laminin, gamma 1 " encoded by a nucleic acid that hybridizes to the "Laminin, gamma 1 " nucleic acid or its complement under low stringency conditions, and/or

(xv) "MT-ACT48" (SEQ ID No:89) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MT-ACT48" encoded by a nucleic acid that hybridizes to the "MT-ACT48" nucleic acid or its complement under low stringency conditions, and/or

(xvi) "NOTCH4-like protein (Hypothetical protein)" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NOTCH4-like protein (Hypothetical protein)" encoded by a nucleic acid that hybridizes to the "NOTCH4-like protein (Hypothetical protein)" nucleic acid or its complement under low stringency conditions, and/or

(xvii) "Neurotrypsin" (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin"

encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions, and/or

(xviii) "PCDH16" (SEQ ID No:92) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDH16" encoded by a nucleic acid that hybridizes to the "PCDH16" nucleic acid or its complement under low stringency conditions, and/or

(xix) "PLOD" (SEQ ID No:93) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PLOD" encoded by a nucleic acid that hybridizes to the "PLOD" nucleic acid or its complement under low stringency conditions, and/or

(xx) "PLOD3" (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PLOD3" encoded by a nucleic acid that hybridizes to the "PLOD3" nucleic acid or its complement under low stringency conditions, and/or

(xxi) "PUTATIVE DNA POLYMERASE DELTA P38 SUBUNIT" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PUTATIVE DNA POLYMERASE DELTA P38 SUBUNIT" encoded by a nucleic acid that hybridizes to the "PUTATIVE DNA POLYMERASE DELTA P38 SUBUNIT" nucleic acid or its complement under low stringency conditions, and/or

(xxii) "RAB39, MEMBER RAS ONCOGENE FAMILY" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB39, MEMBER RAS ONCOGENE FAMILY" encoded by a nucleic acid that hybridizes to the "RAB39, MEMBER RAS ONCOGENE FAMILY" nucleic acid or its complement under low stringency conditions, and/or

(xxiii) "Reelin" (SEQ ID No:97) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Reelin" encoded by a nucleic acid that hybridizes to the "Reelin" nucleic acid or its complement under low stringency conditions, and/or

(xxiv) "SC65" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SC65" encoded by a nucleic acid that hybridizes to the "SC65" nucleic acid or its complement under low stringency conditions, and/or

- (xxv) "Similar to RIKEN cDNA 1300010F03 gene" (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to RIKEN cDNA 1300010F03 gene" encoded by a nucleic acid that hybridizes to the "Similar to RIKEN cDNA 1300010F03 gene" nucleic acid or its complement under low stringency conditions, and/or
- (xxvi) "Similar to hydroxysteroid 17-beta dehydrogenase 11" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to hydroxysteroid 17-beta dehydrogenase 11" encoded by a nucleic acid that hybridizes to the "Similar to hydroxysteroid 17-beta dehydrogenase 11" nucleic acid or its complement under low stringency conditions, and/or
- (xxvii) "Similar to hypothetical protein FLJ22329" (SEQ ID No:101) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to hypothetical protein FLJ22329" encoded by a nucleic acid that hybridizes to the "Similar to hypothetical protein FLJ22329" nucleic acid or its complement under low stringency conditions, and/or
- (xxviii) "UGCGL2" (SEQ ID No:102) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "UGCGL2" encoded by a nucleic acid that hybridizes to the "UGCGL2" nucleic acid or its complement under low stringency conditions, and/or
- (xxix) "hyou1: hypoxia up-regulated 1" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hyou1: hypoxia up-regulated 1" encoded by a nucleic acid that hybridizes to the "hyou1: hypoxia up-regulated 1" nucleic acid or its complement under low stringency conditions, and/or
- (xxx) "q8wvi0" (SEQ ID No:104) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "q8wvi0" encoded by a nucleic acid that hybridizes to the "q8wvi0" nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as

neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42 , wherein said disease or disorder involves increased levels of the amount or activity of said complex.

45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins

- (i) "ADAMTS1" (SEQ ID No:75) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS1" encoded by a nucleic acid that hybridizes to the "ADAMTS1" nucleic acid or its complement under low stringency conditions,
- (ii) "ADAMTS19" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS19" encoded by a nucleic acid that hybridizes to the "ADAMTS19" nucleic acid or its complement under low stringency conditions,

- (iii) "ADAMTS7" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS7" encoded by a nucleic acid that hybridizes to the "ADAMTS7" nucleic acid or its complement under low stringency conditions,
- (iv) "CHRNA5" (SEQ ID No:78) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CHRNA5" encoded by a nucleic acid that hybridizes to the "CHRNA5" nucleic acid or its complement under low stringency conditions,
- (v) "CRTAP" (SEQ ID No:79) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CRTAP" encoded by a nucleic acid that hybridizes to the "CRTAP" nucleic acid or its complement under low stringency conditions,
- (vi) "CU70_HUMAN" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CU70_HUMAN" encoded by a nucleic acid that hybridizes to the "CU70_HUMAN" nucleic acid or its complement under low stringency conditions,
- (vii) "DECR1" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DECR1" encoded by a nucleic acid that hybridizes to the "DECR1" nucleic acid or its complement under low stringency conditions,
- (viii) "DNAJC3" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNAJC3" encoded by a nucleic acid that hybridizes to the "DNAJC3" nucleic acid or its complement under low stringency conditions,
- (ix) "ERP70" (SEQ ID No:83) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ERP70" encoded by a nucleic acid that hybridizes to the "ERP70" nucleic acid or its complement under low stringency conditions,
- (x) "GBTS1" (SEQ ID No:84) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GBTS1" encoded by a nucleic acid that hybridizes to the "GBTS1" nucleic acid or its complement under low stringency conditions,
- (xi) "GRCB" (SEQ ID No:85) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GRCB" encoded by a

nucleic acid that hybridizes to the "GRCB" nucleic acid or its complement under low stringency conditions,

(xii) "Hypothetical protein KIAA1402 (Fragment)" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA1402 (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA1402 (Fragment)" nucleic acid or its complement under low stringency conditions,

(xiii) "LAMB1" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LAMB1" encoded by a nucleic acid that hybridizes to the "LAMB1" nucleic acid or its complement under low stringency conditions,

(xiv) "Laminin, gamma 1 " (SEQ ID No:88) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Laminin, gamma 1 " encoded by a nucleic acid that hybridizes to the "Laminin, gamma 1 " nucleic acid or its complement under low stringency conditions,

(xv) "MT-ACT48" (SEQ ID No:89) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MT-ACT48" encoded by a nucleic acid that hybridizes to the "MT-ACT48" nucleic acid or its complement under low stringency conditions,

(xvi) "NOTCH4-like protein (Hypothetical protein)" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NOTCH4-like protein (Hypothetical protein)" encoded by a nucleic acid that hybridizes to the "NOTCH4-like protein (Hypothetical protein)" nucleic acid or its complement under low stringency conditions,

(xvii) "Neurotrypsin" (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,

(xviii) "PCDH16" (SEQ ID No:92) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDH16" encoded by a nucleic acid that hybridizes to the "PCDH16" nucleic acid or its complement under low stringency conditions,

(xix) "PLOD" (SEQ ID No:93) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PLOD" encoded by a

nucleic acid that hybridizes to the "PLOD" nucleic acid or its complement under low stringency conditions,

(xx) "PLOD3" (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PLOD3" encoded by a nucleic acid that hybridizes to the "PLOD3" nucleic acid or its complement under low stringency conditions,

(xxi) "PUTATIVE DNA POLYMERASE DELTA P38 SUBUNIT" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PUTATIVE DNA POLYMERASE DELTA P38 SUBUNIT" encoded by a nucleic acid that hybridizes to the "PUTATIVE DNA POLYMERASE DELTA P38 SUBUNIT" nucleic acid or its complement under low stringency conditions,

(xxii) "RAB39, MEMBER RAS ONCOGENE FAMILY" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB39, MEMBER RAS ONCOGENE FAMILY" encoded by a nucleic acid that hybridizes to the "RAB39, MEMBER RAS ONCOGENE FAMILY" nucleic acid or its complement under low stringency conditions,

(xxiii) "Reelin" (SEQ ID No:97) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Reelin" encoded by a nucleic acid that hybridizes to the "Reelin" nucleic acid or its complement under low stringency conditions,

(xxiv) "SC65" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SC65" encoded by a nucleic acid that hybridizes to the "SC65" nucleic acid or its complement under low stringency conditions,

(xxv) "Similar to RIKEN cDNA 1300010F03 gene" (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to RIKEN cDNA 1300010F03 gene" encoded by a nucleic acid that hybridizes to the "Similar to RIKEN cDNA 1300010F03 gene" nucleic acid or its complement under low stringency conditions,

(xxvi) "Similar to hydroxysteroid 17-beta dehydrogenase 11" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to hydroxysteroid 17-beta dehydrogenase 11"

encoded by a nucleic acid that hybridizes to the "Similar to hydroxysteroid 17-beta dehydrogenase 11" nucleic acid or its complement under low stringency conditions, (xxvii) "Similar to hypothetical protein FLJ22329" (SEQ ID No:101) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to hypothetical protein FLJ22329" encoded by a nucleic acid that hybridizes to the "Similar to hypothetical protein FLJ22329" nucleic acid or its complement under low stringency conditions, (xxviii) "UGCGL2" (SEQ ID No:102) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "UGCGL2" encoded by a nucleic acid that hybridizes to the "UGCGL2" nucleic acid or its complement under low stringency conditions, (xxix) "hyou1: hypoxia up-regulated 1" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hyou1: hypoxia up-regulated 1" encoded by a nucleic acid that hybridizes to the "hyou1: hypoxia up-regulated 1" nucleic acid or its complement under low stringency conditions, and/or(xxx) "q8wwi0" (SEQ ID No:104) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "q8wwi0" encoded by a nucleic acid that hybridizes to the "q8wwi0" nucleic acid or its complement under low stringency conditions, as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

The invention further relates to the following embodiments of the Hunc18a-complex

1. A protein complex selected from complex (I) and comprising
 - (a) at least one first protein selected from the group consisting of:
 - (i) "Epim" (SEQ ID No:106) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Epim" encoded by a nucleic acid that hybridizes to the "Epim" nucleic acid or its complement under low stringency conditions,
 - (ii) "Hunc18a" (SEQ ID No:110) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hunc18a"

encoded by a nucleic acid that hybridizes to the "Hunc18a" nucleic acid or its complement under low stringency conditions,

(iii) "STX1A" (SEQ ID No:112) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX1A" encoded by a nucleic acid that hybridizes to the "STX1A" nucleic acid or its complement under low stringency conditions,

(iv) "STX1B2" (SEQ ID No:113) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX1B2" encoded by a nucleic acid that hybridizes to the "STX1B2" nucleic acid or its complement under low stringency conditions,

(v) "STX3A" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX3A" encoded by a nucleic acid that hybridizes to the "STX3A" nucleic acid or its complement under low stringency conditions,

(vi) "X11alpha" (SEQ ID No:115) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11alpha" encoded by a nucleic acid that hybridizes to the "X11alpha" nucleic acid or its complement under low stringency conditions, and

(vii) "X11beta" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, and

(b) at least one second protein, which second protein is selected from the group consisting of:

(i) "ELAVL1" (SEQ ID No:105) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ELAVL1" encoded by a nucleic acid that hybridizes to the "ELAVL1" nucleic acid or its complement under low stringency conditions,

(ii) "FIGF" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FIGF" encoded by a nucleic acid that hybridizes to the "FIGF" nucleic acid or its complement under low stringency conditions,

(iii) "Filamin, gamma" (SEQ ID No:108) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Filamin,

gamma" encoded by a nucleic acid that hybridizes to the "Filamin, gamma" nucleic acid or its complement under low stringency conditions,

(iv) "GOLGA3" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GOLGA3" encoded by a nucleic acid that hybridizes to the "GOLGA3" nucleic acid or its complement under low stringency conditions,

(v) "PAWR" (SEQ ID No:111) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PAWR" encoded by a nucleic acid that hybridizes to the "PAWR" nucleic acid or its complement under low stringency conditions, and

(vi) "hypothetical protein BC013764" (SEQ ID No:116) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein BC013764" encoded by a nucleic acid that hybridizes to the "hypothetical protein BC013764" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

2. The protein complex according to No. 1 wherein the first protein is the protein Hunc18a (SEQ ID NO. 110), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of 'Hunc18a' encoded by a nucleic acid that hybridizes to the 'Hunc18a' under low stringency conditions.

3. The protein complex according to No. 1 selected from complex (I) and comprising the following proteins:

(i) "ELAVL1" (SEQ ID No:105) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ELAVL1" encoded by a nucleic acid that hybridizes to the "ELAVL1" nucleic acid or its complement under low stringency conditions,

- (ii) "Epim" (SEQ ID No:106) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Epim" encoded by a nucleic acid that hybridizes to the "Epim" nucleic acid or its complement under low stringency conditions,
- (iii) "FIGF" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FIGF" encoded by a nucleic acid that hybridizes to the "FIGF" nucleic acid or its complement under low stringency conditions,
- (iv) "Filamin, gamma" (SEQ ID No:108) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Filamin, gamma" encoded by a nucleic acid that hybridizes to the "Filamin, gamma" nucleic acid or its complement under low stringency conditions,
- (v) "GOLGA3" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GOLGA3" encoded by a nucleic acid that hybridizes to the "GOLGA3" nucleic acid or its complement under low stringency conditions,
- (vi) "Hunc18a" (SEQ ID No:110) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hunc18a" encoded by a nucleic acid that hybridizes to the "Hunc18a" nucleic acid or its complement under low stringency conditions,
- (vii) "PAWR" (SEQ ID No:111) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PAWR" encoded by a nucleic acid that hybridizes to the "PAWR" nucleic acid or its complement under low stringency conditions,
- (viii) "STX1A" (SEQ ID No:112) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX1A" encoded by a nucleic acid that hybridizes to the "STX1A" nucleic acid or its complement under low stringency conditions,
- (ix) "STX1B2" (SEQ ID No:113) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX1B2" encoded by a nucleic acid that hybridizes to the "STX1B2" nucleic acid or its complement under low stringency conditions,
- (x) "STX3A" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX3A" encoded by a

nucleic acid that hybridizes to the "STX3A" nucleic acid or its complement under low stringency conditions,

(xi) "X11alpha" (SEQ ID No:115) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11alpha" encoded by a nucleic acid that hybridizes to the "X11alpha" nucleic acid or its complement under low stringency conditions,

(xii) "X11beta" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, and/or

(xiii) "hypothetical protein BC013764" (SEQ ID No:116) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein BC013764" encoded by a nucleic acid that hybridizes to the "hypothetical protein BC013764" nucleic acid or its complement under low stringency conditions,

and a protein complex selected from complex (II) and comprising the following proteins:

(i) "ELAVL1" (SEQ ID No:105) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ELAVL1" encoded by a nucleic acid that hybridizes to the "ELAVL1" nucleic acid or its complement under low stringency conditions,

(ii) "Epim" (SEQ ID No:106) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Epim" encoded by a nucleic acid that hybridizes to the "Epim" nucleic acid or its complement under low stringency conditions,

(iii) "FIGF" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FIGF" encoded by a nucleic acid that hybridizes to the "FIGF" nucleic acid or its complement under low stringency conditions,

(iv) "Filamin, gamma" (SEQ ID No:108) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Filamin, gamma" encoded by a nucleic acid that hybridizes to the "Filamin, gamma" nucleic acid or its complement under low stringency conditions,

(v) "GOLGA3" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GOLGA3"

encoded by a nucleic acid that hybridizes to the "GOLGA3" nucleic acid or its complement under low stringency conditions,

(vi) "Hunc18a" (SEQ ID No:110) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hunc18a" encoded by a nucleic acid that hybridizes to the "Hunc18a" nucleic acid or its complement under low stringency conditions,

(vii) "PAWR" (SEQ ID No:111) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PAWR" encoded by a nucleic acid that hybridizes to the "PAWR" nucleic acid or its complement under low stringency conditions,

(viii) "STX1A" (SEQ ID No:112) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX1A" encoded by a nucleic acid that hybridizes to the "STX1A" nucleic acid or its complement under low stringency conditions,

(ix) "STX1B2" (SEQ ID No:113) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX1B2" encoded by a nucleic acid that hybridizes to the "STX1B2" nucleic acid or its complement under low stringency conditions,

(x) "STX3A" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX3A" encoded by a nucleic acid that hybridizes to the "STX3A" nucleic acid or its complement under low stringency conditions, and/or

(xi) "hypothetical protein BC013764" (SEQ ID No:116) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein BC013764" encoded by a nucleic acid that hybridizes to the "hypothetical protein BC013764" nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 5 of the following proteins:

(i) "ELAVL1" (SEQ ID No:105) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ELAVL1" encoded by a nucleic acid that hybridizes to the "ELAVL1" nucleic acid or its complement under low stringency conditions,

- (ii) "Epim" (SEQ ID No:106) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Epim" encoded by a nucleic acid that hybridizes to the "Epim" nucleic acid or its complement under low stringency conditions,
- (iii) "FIGF" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FIGF" encoded by a nucleic acid that hybridizes to the "FIGF" nucleic acid or its complement under low stringency conditions,
- (iv) "Filamin, gamma" (SEQ ID No:108) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Filamin, gamma" encoded by a nucleic acid that hybridizes to the "Filamin, gamma" nucleic acid or its complement under low stringency conditions,
- (v) "GOLGA3" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GOLGA3" encoded by a nucleic acid that hybridizes to the "GOLGA3" nucleic acid or its complement under low stringency conditions,
- (vi) "Hunc18a" (SEQ ID No:110) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hunc18a" encoded by a nucleic acid that hybridizes to the "Hunc18a" nucleic acid or its complement under low stringency conditions,
- (vii) "PAWR" (SEQ ID No:111) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PAWR" encoded by a nucleic acid that hybridizes to the "PAWR" nucleic acid or its complement under low stringency conditions,
- (viii) "STX1A" (SEQ ID No:112) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX1A" encoded by a nucleic acid that hybridizes to the "STX1A" nucleic acid or its complement under low stringency conditions,
- (ix) "STX1B2" (SEQ ID No:113) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX1B2" encoded by a nucleic acid that hybridizes to the "STX1B2" nucleic acid or its complement under low stringency conditions,
- (x) "STX3A" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX3A" encoded by a

nucleic acid that hybridizes to the "STX3A" nucleic acid or its complement under low stringency conditions,

(xi) "X11alpha" (SEQ ID No:115) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11alpha" encoded by a nucleic acid that hybridizes to the "X11alpha" nucleic acid or its complement under low stringency conditions,

(xii) "X11beta" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions,

(xiii) "hypothetical protein BC013764" (SEQ ID No:116) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein BC013764" encoded by a nucleic acid that hybridizes to the "hypothetical protein BC013764" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.

6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.

7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.

8. The complex of any of No. 1 - 7 that is involved in the transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the

expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).

9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps: expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.

10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.

11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.

12. Component of the Hunc18a obtainable by a process according to any of No. 9 - 11.

13. Protein of the Hunc18a selected from

- (i) "GOLGA3" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GOLGA3" encoded by a nucleic acid that hybridizes to the "GOLGA3" nucleic acid or its complement under low stringency conditions, and
- (ii) "hypothetical protein BC013764" (SEQ ID No:116) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein BC013764" encoded by a nucleic acid that hybridizes to the "hypothetical protein BC013764" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer

comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

14. Nucleic acid encoding a protein according to No. 13.

15. Construct, preferably a vector construct, comprising (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or

(b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).

16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).

17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.

18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.
19. The kit according to No. 18 for processing a substrate of said complex.
20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative disease such as Alzheimer's disease and related disorders; .
21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.
22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.
23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:
 - (i) "GOLGA3" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GOLGA3" encoded by a nucleic acid that hybridizes to the "GOLGA3" nucleic acid or its complement under low stringency conditions, and/or
 - (ii) "hypothetical protein BC013764" (SEQ ID No:116) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein BC013764" encoded by a nucleic acid that hybridizes to the "hypothetical protein BC013764" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.
24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative disease such as Alzheimer's disease and related disorders; .

25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:

- (i) "GOLGA3" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GOLGA3" encoded by a nucleic acid that hybridizes to the "GOLGA3" nucleic acid or its complement under low stringency conditions, and/or
- (ii) "hypothetical protein BC013764" (SEQ ID No:116) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein BC013764" encoded by a nucleic acid that hybridizes to the "hypothetical protein BC013764" nucleic acid or its complement under low stringency conditions, comprising the steps of
 - (a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and
 - (b) determinig whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of(a) exposing said complex, or a cell or organism containing Hunc18a to one or more candidate molecules; and

- (b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.
28. The method of No. 26, wherein the activity of said complex is determined.
29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.
30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.
31. The method of No. 30, wherein said determining step comprises determining whether
 - (i) "ELAVL1" (SEQ ID No:105) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ELAVL1" encoded by a nucleic acid that hybridizes to the "ELAVL1" nucleic acid or its complement under low stringency conditions, and/or
 - (ii) "Epim" (SEQ ID No:106) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Epim" encoded by a nucleic acid that hybridizes to the "Epim" nucleic acid or its complement under low stringency conditions, and/or
 - (iii) "FIGF" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FIGF" encoded by a nucleic acid that hybridizes to the "FIGF" nucleic acid or its complement under low stringency conditions, and/or
 - (iv) "Filamin, gamma" (SEQ ID No:108) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Filamin, gamma" encoded by a nucleic acid that hybridizes to the "Filamin, gamma" nucleic acid or its complement under low stringency conditions, and/or
 - (v) "GOLGA3" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GOLGA3" encoded by a nucleic acid that hybridizes to the "GOLGA3" nucleic acid or its complement under low stringency conditions, and/or

- (vi) "Hunc18a" (SEQ ID No:110) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hunc18a" encoded by a nucleic acid that hybridizes to the "Hunc18a" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "PAWR" (SEQ ID No:111) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PAWR" encoded by a nucleic acid that hybridizes to the "PAWR" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "STX1A" (SEQ ID No:112) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX1A" encoded by a nucleic acid that hybridizes to the "STX1A" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "STX1B2" (SEQ ID No:113) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX1B2" encoded by a nucleic acid that hybridizes to the "STX1B2" nucleic acid or its complement under low stringency conditions, and/or
- (x) "STX3A" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX3A" encoded by a nucleic acid that hybridizes to the "STX3A" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "X11alpha" (SEQ ID No:115) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11alpha" encoded by a nucleic acid that hybridizes to the "X11alpha" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "X11beta" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "hypothetical protein BC013764" (SEQ ID No:116) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein BC013764" encoded by a nucleic acid that hybridizes to the "hypothetical protein BC013764" nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease and related disorders; .
33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease and related disorders; .
34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.
35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.
36. The method of No. 35, wherein the amount of said complex is determined.
37. The method of No. 35, wherein the activity of said complex is determined.
38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said

complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

40. The method of No. 39, wherein said determining step comprises determining whether
(i) "ELAVL1" (SEQ ID No:105) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ELAVL1" encoded by a nucleic acid that hybridizes to the "ELAVL1" nucleic acid or its complement under low stringency conditions, and/or
(ii) "Epim" (SEQ ID No:106) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Epim" encoded by a nucleic acid that hybridizes to the "Epim" nucleic acid or its complement under low stringency conditions, and/or
(iii) "FIGF" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FIGF" encoded by a nucleic acid that hybridizes to the "FIGF" nucleic acid or its complement under low stringency conditions, and/or
(iv) "Filamin, gamma" (SEQ ID No:108) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Filamin, gamma" encoded by a nucleic acid that hybridizes to the "Filamin, gamma" nucleic acid or its complement under low stringency conditions, and/or
(v) "GOLGA3" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GOLGA3" encoded by a nucleic acid that hybridizes to the "GOLGA3" nucleic acid or its complement under low stringency conditions, and/or
(vi) "Hunc18a" (SEQ ID No:110) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hunc18a" encoded by a nucleic acid that hybridizes to the "Hunc18a" nucleic acid or its complement under low stringency conditions, and/or
(vii) "PAWR" (SEQ ID No:111) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PAWR" encoded by a

nucleic acid that hybridizes to the "PAWR" nucleic acid or its complement under low stringency conditions, and/or

(viii) "STX1A" (SEQ ID No:112) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX1A" encoded by a nucleic acid that hybridizes to the "STX1A" nucleic acid or its complement under low stringency conditions, and/or

(ix) "STX1B2" (SEQ ID No:113) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX1B2" encoded by a nucleic acid that hybridizes to the "STX1B2" nucleic acid or its complement under low stringency conditions, and/or

(x) "STX3A" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX3A" encoded by a nucleic acid that hybridizes to the "STX3A" nucleic acid or its complement under low stringency conditions, and/or

(xi) "X11alpha" (SEQ ID No:115) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11alpha" encoded by a nucleic acid that hybridizes to the "X11alpha" nucleic acid or its complement under low stringency conditions, and/or

(xii) "X11beta" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, and/or

(xiii) "hypothetical protein BC013764" (SEQ ID No:116) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein BC013764" encoded by a nucleic acid that hybridizes to the "hypothetical protein BC013764" nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative disease such as Alzheimer's disease and related disorders; .

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42 , wherein said disease or disorder involves increased levels of the amount or activity of said complex.

45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins
(i) "ELAVL1" (SEQ ID No:105) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ELAVL1" encoded by a nucleic acid that hybridizes to the "ELAVL1" nucleic acid or its complement under low stringency conditions,
(ii) "Epim" (SEQ ID No:106) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Epim" encoded by a nucleic acid that hybridizes to the "Epim" nucleic acid or its complement under low stringency conditions,
(iii) "FIGF" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FIGF" encoded by a

nucleic acid that hybridizes to the "FIGF" nucleic acid or its complement under low stringency conditions,

(iv) "Filamin, gamma" (SEQ ID No:108) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Filamin, gamma" encoded by a nucleic acid that hybridizes to the "Filamin, gamma" nucleic acid or its complement under low stringency conditions,

(v) "GOLGA3" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GOLGA3" encoded by a nucleic acid that hybridizes to the "GOLGA3" nucleic acid or its complement under low stringency conditions,

(vi) "Hunc18a" (SEQ ID No:110) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hunc18a" encoded by a nucleic acid that hybridizes to the "Hunc18a" nucleic acid or its complement under low stringency conditions,

(vii) "PAWR" (SEQ ID No:111) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PAWR" encoded by a nucleic acid that hybridizes to the "PAWR" nucleic acid or its complement under low stringency conditions,

(viii) "STX1A" (SEQ ID No:112) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX1A" encoded by a nucleic acid that hybridizes to the "STX1A" nucleic acid or its complement under low stringency conditions,

(ix) "STX1B2" (SEQ ID No:113) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX1B2" encoded by a nucleic acid that hybridizes to the "STX1B2" nucleic acid or its complement under low stringency conditions,

(x) "STX3A" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX3A" encoded by a nucleic acid that hybridizes to the "STX3A" nucleic acid or its complement under low stringency conditions,

(xi) "X11alpha" (SEQ ID No:115) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11alpha" encoded by a nucleic acid that hybridizes to the "X11alpha" nucleic acid or its complement under low stringency conditions,

(xii) "X11beta" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, and/or(xiii) "hypothetical protein BC013764" (SEQ ID No:116) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein BC013764" encoded by a nucleic acid that hybridizes to the "hypothetical protein BC013764" nucleic acid or its complement under low stringency conditions,as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease and related disorders; .

The invention further relates to the following embodiments of the Telencephalin-complex

1. A protein complex selected from complex (I) and comprising

(a) at least one first protein selected from the group consisting of:

(i) "CD11a/CD18 INTEGRIN, BETA-2" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CD11a/CD18 INTEGRIN, BETA-2" encoded by a nucleic acid that hybridizes to the "CD11a/CD18 INTEGRIN, BETA-2" nucleic acid or its complement under low stringency conditions,

(ii) "Presenilin 1" (SEQ ID No:123) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions, and

(iii) "Telencephalin" (SEQ ID No:126) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Telencephalin" encoded by a nucleic acid that hybridizes to the "Telencephalin" nucleic acid or its complement under low stringency conditions, and

(b) at least one second protein, which second protein is selected from the group consisting of:

(i) "APOD" (SEQ ID No:117) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APOD" encoded by a

nucleic acid that hybridizes to the "APOD" nucleic acid or its complement under low stringency conditions,

(ii) "CALD1" (SEQ ID No:118) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CALD1" encoded by a nucleic acid that hybridizes to the "CALD1" nucleic acid or its complement under low stringency conditions,

(iii) "CALR" (SEQ ID No:119) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CALR" encoded by a nucleic acid that hybridizes to the "CALR" nucleic acid or its complement under low stringency conditions,

(iv) "CHRNA5" (SEQ ID No:78) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CHRNA5" encoded by a nucleic acid that hybridizes to the "CHRNA5" nucleic acid or its complement under low stringency conditions,

(v) "HYPOTHETICAL PROTEIN FLJ35393" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ35393" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ35393" nucleic acid or its complement under low stringency conditions,

(vi) "OPA1" (SEQ ID No:121) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "OPA1" encoded by a nucleic acid that hybridizes to the "OPA1" nucleic acid or its complement under low stringency conditions,

(vii) "PYCS" (SEQ ID No:122) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PYCS" encoded by a nucleic acid that hybridizes to the "PYCS" nucleic acid or its complement under low stringency conditions,

(viii) "RAB6A" (SEQ ID No:124) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB6A" encoded by a nucleic acid that hybridizes to the "RAB6A" nucleic acid or its complement under low stringency conditions, and

(ix) "RAP1, GTP-GDP dissociation stimulator 1" (SEQ ID No:125) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAP1, GTP-GDP dissociation stimulator 1" encoded by a nucleic acid that

hybridizes to the "RAP1, GTP-GDP dissociation stimulator 1" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

2. The protein complex according to No. 1 wherein the first protein is the protein Telencephalin (SEQ ID NO. 126), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of 'Telencephalin' encoded by a nucleic acid that hybridizes to the 'Telencephalin' under low stringency conditions.

3. The protein complex according to No. 1 selected from complex (I) and comprising the following proteins:

- (i) "APOD" (SEQ ID No:117) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APOD" encoded by a nucleic acid that hybridizes to the "APOD" nucleic acid or its complement under low stringency conditions,
- (ii) "CALD1" (SEQ ID No:118) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CALD1" encoded by a nucleic acid that hybridizes to the "CALD1" nucleic acid or its complement under low stringency conditions,
- (iii) "CALR" (SEQ ID No:119) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CALR" encoded by a nucleic acid that hybridizes to the "CALR" nucleic acid or its complement under low stringency conditions,
- (iv) "CD11a/CD18 INTEGRIN, BETA-2" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CD11a/CD18 INTEGRIN, BETA-2" encoded by a nucleic acid that hybridizes

to the "CD11a/CD18 INTEGRIN, BETA-2" nucleic acid or its complement under low stringency conditions,

(v) "CHRNA5" (SEQ ID No:78) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CHRNA5" encoded by a nucleic acid that hybridizes to the "CHRNA5" nucleic acid or its complement under low stringency conditions,

(vi) "HYPOTHETICAL PROTEIN FLJ35393" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ35393" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ35393" nucleic acid or its complement under low stringency conditions,

(vii) "OPA1" (SEQ ID No:121) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "OPA1" encoded by a nucleic acid that hybridizes to the "OPA1" nucleic acid or its complement under low stringency conditions,

(viii) "PYCS" (SEQ ID No:122) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PYCS" encoded by a nucleic acid that hybridizes to the "PYCS" nucleic acid or its complement under low stringency conditions,

(ix) "Presenilin 1" (SEQ ID No:123) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions,

(x) "RAB6A" (SEQ ID No:124) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB6A" encoded by a nucleic acid that hybridizes to the "RAB6A" nucleic acid or its complement under low stringency conditions,

(xi) "RAP1, GTP-GDP dissociation stimulator 1" (SEQ ID No:125) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAP1, GTP-GDP dissociation stimulator 1" encoded by a nucleic acid that hybridizes to the "RAP1, GTP-GDP dissociation stimulator 1" nucleic acid or its complement under low stringency conditions, and/or

(xii) "Telencephalin" (SEQ ID No:126) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Telencephalin"

encoded by a nucleic acid that hybridizes to the "Telencephalin" nucleic acid or its complement under low stringency conditions, and a protein complex selected from complex (II) and comprising the following proteins:

- (i) "APOD" (SEQ ID No:117) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APOD" encoded by a nucleic acid that hybridizes to the "APOD" nucleic acid or its complement under low stringency conditions,
- (ii) "CALD1" (SEQ ID No:118) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CALD1" encoded by a nucleic acid that hybridizes to the "CALD1" nucleic acid or its complement under low stringency conditions,
- (iii) "CALR" (SEQ ID No:119) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CALR" encoded by a nucleic acid that hybridizes to the "CALR" nucleic acid or its complement under low stringency conditions,
- (iv) "CHRNA5" (SEQ ID No:78) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CHRNA5" encoded by a nucleic acid that hybridizes to the "CHRNA5" nucleic acid or its complement under low stringency conditions,
- (v) "HYPOTHETICAL PROTEIN FLJ35393" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ35393" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ35393" nucleic acid or its complement under low stringency conditions,
- (vi) "OPA1" (SEQ ID No:121) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "OPA1" encoded by a nucleic acid that hybridizes to the "OPA1" nucleic acid or its complement under low stringency conditions,
- (vii) "PYCS" (SEQ ID No:122) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PYCS" encoded by a nucleic acid that hybridizes to the "PYCS" nucleic acid or its complement under low stringency conditions,
- (viii) "RAB6A" (SEQ ID No:124) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB6A"

encoded by a nucleic acid that hybridizes to the "RAB6A" nucleic acid or its complement under low stringency conditions,

(ix) "RAP1, GTP-GDP dissociation stimulator 1" (SEQ ID No:125) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAP1, GTP-GDP dissociation stimulator 1" encoded by a nucleic acid that hybridizes to the "RAP1, GTP-GDP dissociation stimulator 1" nucleic acid or its complement under low stringency conditions, and/or

(x) "Telencephalin" (SEQ ID No:126) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Telencephalin" encoded by a nucleic acid that hybridizes to the "Telencephalin" nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 8 of the following proteins:

(i) "APOD" (SEQ ID No:117) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APOD" encoded by a nucleic acid that hybridizes to the "APOD" nucleic acid or its complement under low stringency conditions,

(ii) "CALD1" (SEQ ID No:118) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CALD1" encoded by a nucleic acid that hybridizes to the "CALD1" nucleic acid or its complement under low stringency conditions,

(iii) "CALR" (SEQ ID No:119) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CALR" encoded by a nucleic acid that hybridizes to the "CALR" nucleic acid or its complement under low stringency conditions,

(iv) "CD11a/CD18 INTEGRIN, BETA-2" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CD11a/CD18 INTEGRIN, BETA-2" encoded by a nucleic acid that hybridizes to the "CD11a/CD18 INTEGRIN, BETA-2" nucleic acid or its complement under low stringency conditions,

(v) "CHRNA5" (SEQ ID No:78) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CHRNA5" encoded by a

nucleic acid that hybridizes to the "CHRNA5" nucleic acid or its complement under low stringency conditions,

(vi) "HYPOTHETICAL PROTEIN FLJ35393" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ35393" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ35393" nucleic acid or its complement under low stringency conditions,

(vii) "OPA1" (SEQ ID No:121) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "OPA1" encoded by a nucleic acid that hybridizes to the "OPA1" nucleic acid or its complement under low stringency conditions,

(viii) "PYCS" (SEQ ID No:122) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PYCS" encoded by a nucleic acid that hybridizes to the "PYCS" nucleic acid or its complement under low stringency conditions,

(ix) "Presenilin 1" (SEQ ID No:123) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions,

(x) "RAB6A" (SEQ ID No:124) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB6A" encoded by a nucleic acid that hybridizes to the "RAB6A" nucleic acid or its complement under low stringency conditions,

(xi) "RAP1, GTP-GDP dissociation stimulator 1" (SEQ ID No:125) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAP1, GTP-GDP dissociation stimulator 1" encoded by a nucleic acid that hybridizes to the "RAP1, GTP-GDP dissociation stimulator 1" nucleic acid or its complement under low stringency conditions,

(xii) "Telencephalin" (SEQ ID No:126) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Telencephalin" encoded by a nucleic acid that hybridizes to the "Telencephalin" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.
6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.
7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.
8. The complex of any of No. 1 - 7 that is involved in the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).
9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps: expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.

10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.
11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.
12. Component of the Telencephalin obtainable by a process according to any of No. 9 - 11.
13. Protein of the Telencephalin selected from
 - (i) "HYPOTHETICAL PROTEIN FLJ35393" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ35393" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ35393" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.
14. Nucleic acid encoding a protein according to No. 13.
15. Construct, preferably a vector construct, comprising (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or
(b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).

16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).
17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.
18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.
19. The kit according to No. 18 for processing a substrate of said complex.
20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.
21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.
22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.

23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:

(i) "HYPOTHETICAL PROTEIN FLJ35393" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ35393" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ35393" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:

(i) "HYPOTHETICAL PROTEIN FLJ35393" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ35393" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ35393" nucleic acid or its complement under low stringency conditions, comprising the steps of
(a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and
(b) determinig whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of(a) exposing said complex, or a cell or organism containing Telencephalin to one or more candidate molecules; and

(b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the

presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.
28. The method of No. 26, wherein the activity of said complex is determined.
29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.
30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.
31. The method of No. 30, wherein said determining step comprises determining whether
 - (i) "APOD" (SEQ ID No:117) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APOD" encoded by a nucleic acid that hybridizes to the "APOD" nucleic acid or its complement under low stringency conditions, and/or
 - (ii) "CALD1" (SEQ ID No:118) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CALD1" encoded by a nucleic acid that hybridizes to the "CALD1" nucleic acid or its complement under low stringency conditions, and/or
 - (iii) "CALR" (SEQ ID No:119) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CALR" encoded by a nucleic acid that hybridizes to the "CALR" nucleic acid or its complement under low stringency conditions, and/or

- (iv) "CD11a/CD18 INTEGRIN, BETA-2" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CD11a/CD18 INTEGRIN, BETA-2" encoded by a nucleic acid that hybridizes to the "CD11a/CD18 INTEGRIN, BETA-2" nucleic acid or its complement under low stringency conditions, and/or
- (v) "CHRNA5" (SEQ ID No:78) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CHRNA5" encoded by a nucleic acid that hybridizes to the "CHRNA5" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "HYPOTHETICAL PROTEIN FLJ35393" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ35393" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ35393" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "OPA1" (SEQ ID No:121) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "OPA1" encoded by a nucleic acid that hybridizes to the "OPA1" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "PYCS" (SEQ ID No:122) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PYCS" encoded by a nucleic acid that hybridizes to the "PYCS" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "Presenilin 1" (SEQ ID No:123) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions, and/or
- (x) "RAB6A" (SEQ ID No:124) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB6A" encoded by a nucleic acid that hybridizes to the "RAB6A" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "RAP1, GTP-GDP dissociation stimulator 1" (SEQ ID No:125) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAP1, GTP-GDP dissociation stimulator 1" encoded by a nucleic acid that

hybridizes to the "RAP1, GTP-GDP dissociation stimulator 1" nucleic acid or its complement under low stringency conditions, and/or
(xii) "Telencephalin" (SEQ ID No:126) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Telencephalin" encoded by a nucleic acid that hybridizes to the "Telencephalin" nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.
37. The method of No. 35, wherein the activity of said complex is determined.
38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.
39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.
40. The method of No. 39, wherein said determining step comprises determining whether
 - (i) "APOD" (SEQ ID No:117) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APOP" encoded by a nucleic acid that hybridizes to the "APOP" nucleic acid or its complement under low stringency conditions, and/or
 - (ii) "CALD1" (SEQ ID No:118) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CALD1" encoded by a nucleic acid that hybridizes to the "CALD1" nucleic acid or its complement under low stringency conditions, and/or
 - (iii) "CALR" (SEQ ID No:119) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CALR" encoded by a nucleic acid that hybridizes to the "CALR" nucleic acid or its complement under low stringency conditions, and/or
 - (iv) "CD11a/CD18 INTEGRIN, BETA-2" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CD11a/CD18 INTEGRIN, BETA-2" encoded by a nucleic acid that hybridizes to the "CD11a/CD18 INTEGRIN, BETA-2" nucleic acid or its complement under low stringency conditions, and/or
 - (v) "CHRNA5" (SEQ ID No:78) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CHRNA5" encoded by a

nucleic acid that hybridizes to the "CHRNA5" nucleic acid or its complement under low stringency conditions, and/or

(vi) "HYPOTHETICAL PROTEIN FLJ35393" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ35393" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ35393" nucleic acid or its complement under low stringency conditions, and/or

(vii) "OPA1" (SEQ ID No:121) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "OPA1" encoded by a nucleic acid that hybridizes to the "OPA1" nucleic acid or its complement under low stringency conditions, and/or

(viii) "PYCS" (SEQ ID No:122) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PYCS" encoded by a nucleic acid that hybridizes to the "PYCS" nucleic acid or its complement under low stringency conditions, and/or

(ix) "Presenilin 1" (SEQ ID No:123) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions, and/or

(x) "RAB6A" (SEQ ID No:124) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB6A" encoded by a nucleic acid that hybridizes to the "RAB6A" nucleic acid or its complement under low stringency conditions, and/or

(xi) "RAP1, GTP-GDP dissociation stimulator 1" (SEQ ID No:125) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAP1, GTP-GDP dissociation stimulator 1" encoded by a nucleic acid that hybridizes to the "RAP1, GTP-GDP dissociation stimulator 1" nucleic acid or its complement under low stringency conditions, and/or

(xii) "Telencephalin" (SEQ ID No:126) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Telencephalin" encoded by a nucleic acid that hybridizes to the "Telencephalin" nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42 , wherein said disease or disorder involves increased levels of the amount or activity of said complex.

45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins
(i) "APOD" (SEQ ID No:117) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APOD" encoded by a nucleic acid that hybridizes to the "APOD" nucleic acid or its complement under low stringency conditions,

- (ii) "CALD1" (SEQ ID No:118) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CALD1" encoded by a nucleic acid that hybridizes to the "CALD1" nucleic acid or its complement under low stringency conditions,
- (iii) "CALR" (SEQ ID No:119) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CALR" encoded by a nucleic acid that hybridizes to the "CALR" nucleic acid or its complement under low stringency conditions,
- (iv) "CD11a/CD18 INTEGRIN, BETA-2" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CD11a/CD18 INTEGRIN, BETA-2" encoded by a nucleic acid that hybridizes to the "CD11a/CD18 INTEGRIN, BETA-2" nucleic acid or its complement under low stringency conditions,
- (v) "CHRNA5" (SEQ ID No:78) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CHRNA5" encoded by a nucleic acid that hybridizes to the "CHRNA5" nucleic acid or its complement under low stringency conditions,
- (vi) "HYPOTHETICAL PROTEIN FLJ35393" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ35393" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ35393" nucleic acid or its complement under low stringency conditions,
- (vii) "OPA1" (SEQ ID No:121) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "OPA1" encoded by a nucleic acid that hybridizes to the "OPA1" nucleic acid or its complement under low stringency conditions,
- (viii) "PYCS" (SEQ ID No:122) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PYCS" encoded by a nucleic acid that hybridizes to the "PYCS" nucleic acid or its complement under low stringency conditions,
- (ix) "Presenilin 1" (SEQ ID No:123) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions,

- (x) "RAB6A" (SEQ ID No:124) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB6A" encoded by a nucleic acid that hybridizes to the "RAB6A" nucleic acid or its complement under low stringency conditions,
- (xi) "RAP1, GTP-GDP dissociation stimulator 1" (SEQ ID No:125) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAP1, GTP-GDP dissociation stimulator 1" encoded by a nucleic acid that hybridizes to the "RAP1, GTP-GDP dissociation stimulator 1" nucleic acid or its complement under low stringency conditions, and/or(xii) "Telencephalin" (SEQ ID No:126) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Telencephalin" encoded by a nucleic acid that hybridizes to the "Telencephalin" nucleic acid or its complement under low stringency conditions,as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

The invention further relates to the following embodiments of the PC7-complex

1. A protein complex selected from complex (I) and comprising
 - (a) at least one first protein selected from the group consisting of:
 - (i) "BACE1" (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BACE1" encoded by a nucleic acid that hybridizes to the "BACE1" nucleic acid or its complement under low stringency conditions, and
 - (ii) "PC7" (SEQ ID No:130) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PC7" encoded by a nucleic acid that hybridizes to the "PC7" nucleic acid or its complement under low stringency conditions, and
 - (b) at least one second protein, which second protein is selected from the group consisting of:
 - (i) "15 KDA SELENO- PROTEIN PRECURSOR" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a

variant of "15 KDA SELENO- PROTEIN PRECURSOR" encoded by a nucleic acid that hybridizes to the "15 KDA SELENO- PROTEIN PRECURSOR" nucleic acid or its complement under low stringency conditions,

- (ii) "APP-C99" (SEQ ID No:128) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions,
- (iii) "DNAJC3" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNAJC3" encoded by a nucleic acid that hybridizes to the "DNAJC3" nucleic acid or its complement under low stringency conditions,
- (iv) "Neurotrypsin" (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,
- (v) "PTPN1" (SEQ ID No:131) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PTPN1" encoded by a nucleic acid that hybridizes to the "PTPN1" nucleic acid or its complement under low stringency conditions, and
- (vi) "Protocadherin beta 7 " (SEQ ID No:132) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 7 " encoded by a nucleic acid that hybridizes to the "Protocadherin beta 7 " nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

2. The protein complex according to No. 1 wherein the first protein is the protein PC7 (SEQ ID NO. 130), or a functionally active derivative thereof, or a functionally active

fragment thereof, or a homolog thereof, or a variant of 'PC7' encoded by a nucleic acid that hybridizes to the 'PC7' under low stringency conditions.

3. The protein complex according to No. 1 selected from complex (I) and comprising the following proteins:

- (i) "15 KDA SELENO- PROTEIN PRECURSOR" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "15 KDA SELENO- PROTEIN PRECURSOR" encoded by a nucleic acid that hybridizes to the "15 KDA SELENO- PROTEIN PRECURSOR" nucleic acid or its complement under low stringency conditions,
- (ii) "APP-C99" (SEQ ID No:128) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions,
- (iii) "BACE1" (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BACE1" encoded by a nucleic acid that hybridizes to the "BACE1" nucleic acid or its complement under low stringency conditions,
- (iv) "DNAJC3" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNAJC3" encoded by a nucleic acid that hybridizes to the "DNAJC3" nucleic acid or its complement under low stringency conditions,
- (v) "Neurotrypsin" (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,
- (vi) "PC7" (SEQ ID No:130) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PC7" encoded by a nucleic acid that hybridizes to the "PC7" nucleic acid or its complement under low stringency conditions,
- (vii) "PTPN1" (SEQ ID No:131) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PTPN1" encoded by a nucleic acid that hybridizes to the "PTPN1" nucleic acid or its complement under low stringency conditions, and/or

(viii) "Protocadherin beta 7 " (SEQ ID No:132) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 7 " encoded by a nucleic acid that hybridizes to the "Protocadherin beta 7 " nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 5 of the following proteins:

- (i) "15 KDA SELENO- PROTEIN PRECURSOR" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "15 KDA SELENO- PROTEIN PRECURSOR" encoded by a nucleic acid that hybridizes to the "15 KDA SELENO- PROTEIN PRECURSOR" nucleic acid or its complement under low stringency conditions,
- (ii) "APP-C99" (SEQ ID No:128) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions,
- (iii) "BACE1" (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BACE1" encoded by a nucleic acid that hybridizes to the "BACE1" nucleic acid or its complement under low stringency conditions,
- (iv) "DNAJC3" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNAJC3" encoded by a nucleic acid that hybridizes to the "DNAJC3" nucleic acid or its complement under low stringency conditions,
- (v) "Neurotrypsin" (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,
- (vi) "PC7" (SEQ ID No:130) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PC7" encoded by a nucleic acid that hybridizes to the "PC7" nucleic acid or its complement under low stringency conditions,
- (vii) "PTPN1" (SEQ ID No:131) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PTPN1" encoded by a

nucleic acid that hybridizes to the "PTPN1" nucleic acid or its complement under low stringency conditions,

(viii) "Protocadherin beta 7 " (SEQ ID No:132) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 7 " encoded by a nucleic acid that hybridizes to the "Protocadherin beta 7 " nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.

6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.

7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.

8. The complex of any of No. 1 - 7 that is involved in the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).

9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps: expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.
10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.
11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.
12. Component of the PC7 obtainable by a process according to any of No. 9 - 11.
13. Protein of the PC7 selected from
- (i) "DNAJC3" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNAJC3" encoded by a nucleic acid that hybridizes to the "DNAJC3" nucleic acid or its complement under low stringency conditions, and
 - (ii) "Protocadherin beta 7 " (SEQ ID No:132) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 7 " encoded by a nucleic acid that hybridizes to the "Protocadherin beta 7 " nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.
14. Nucleic acid encoding a protein according to No. 13.

15. Construct, preferably a vector construct, comprising (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or

(b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).

16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).

17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.

18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.

19. The kit according to No. 18 for processing a substrate of said complex.

20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders; .

21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.

22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.

23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:

(i) "DNAJC3" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNAJC3" encoded by a nucleic acid that hybridizes to the "DNAJC3" nucleic acid or its complement under low stringency conditions, and/or

(ii) "Protocadherin beta 7 " (SEQ ID No:132) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 7 " encoded by a nucleic acid that hybridizes to the "Protocadherin beta 7 " nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders; .

25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:

(i) "DNAJC3" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNAJC3" encoded by a nucleic acid that hybridizes to the "DNAJC3" nucleic acid or its complement under low stringency conditions, and/or

- (ii) "Protocadherin beta 7 " (SEQ ID No:132) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 7 " encoded by a nucleic acid that hybridizes to the "Protocadherin beta 7 " nucleic acid or its complement under low stringency conditions, comprising the steps of
- exposing said complex, or a cell or organism containing same to one or more candidate molecules; and
 - determining whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of (a) exposing said complex, or a cell or organism containing PC7 to one or more candidate molecules; and

(b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.

28. The method of No. 26, wherein the activity of said complex is determined.

29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of

said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.

30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.

31. The method of No. 30, wherein said determining step comprises determining whether

(i) "15 KDA SELENO- PROTEIN PRECURSOR" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "15 KDA SELENO- PROTEIN PRECURSOR" encoded by a nucleic acid that hybridizes to the "15 KDA SELENO- PROTEIN PRECURSOR" nucleic acid or its complement under low stringency conditions, and/or

(ii) "APP-C99" (SEQ ID No:128) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions, and/or

(iii) "BACE1" (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BACE1" encoded by a nucleic acid that hybridizes to the "BACE1" nucleic acid or its complement under low stringency conditions, and/or

(iv) "DNAJC3" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNAJC3" encoded by a nucleic acid that hybridizes to the "DNAJC3" nucleic acid or its complement under low stringency conditions, and/or

(v) "Neurotrypsin" (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions, and/or

(vi) "PC7" (SEQ ID No:130) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PC7" encoded by a nucleic acid that hybridizes to the "PC7" nucleic acid or its complement under low stringency conditions, and/or

(vii) "PTPN1" (SEQ ID No:131) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PTPN1" encoded by a

nucleic acid that hybridizes to the "PTPN1" nucleic acid or its complement under low stringency conditions, and/or

(viii) "Protocadherin beta 7 " (SEQ ID No:132) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 7 " encoded by a nucleic acid that hybridizes to the "Protocadherin beta 7 " nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders; .

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders; .

34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.
37. The method of No. 35, wherein the activity of said complex is determined.
38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.
39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.
40. The method of No. 39, wherein said determining step comprises determining whether
 - (i) "15 KDA SELENO- PROTEIN PRECURSOR" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "15 KDA SELENO- PROTEIN PRECURSOR" encoded by a nucleic acid that hybridizes to the "15 KDA SELENO- PROTEIN PRECURSOR" nucleic acid or its complement under low stringency conditions, and/or
 - (ii) "APP-C99" (SEQ ID No:128) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions, and/or
 - (iii) "BACE1" (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BACE1" encoded by a nucleic acid that hybridizes to the "BACE1" nucleic acid or its complement under low stringency conditions, and/or
 - (iv) "DNAJC3" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNAJC3" encoded by a nucleic acid that hybridizes to the "DNAJC3" nucleic acid or its complement under low stringency conditions, and/or

- (v) "Neurotrypsin" (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "PC7" (SEQ ID No:130) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PC7" encoded by a nucleic acid that hybridizes to the "PC7" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "PTPN1" (SEQ ID No:131) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PTPN1" encoded by a nucleic acid that hybridizes to the "PTPN1" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "Protocadherin beta 7 " (SEQ ID No:132) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 7 " encoded by a nucleic acid that hybridizes to the "Protocadherin beta 7 " nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders; .

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of

beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42 , wherein said disease or disorder involves increased levels of the amount or activity of said complex.

45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins
(i) "15 KDA SELENO- PROTEIN PRECURSOR" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "15 KDA SELENO- PROTEIN PRECURSOR" encoded by a nucleic acid that hybridizes to the "15 KDA SELENO- PROTEIN PRECURSOR" nucleic acid or its complement under low stringency conditions,
(ii) "APP-C99" (SEQ ID No:128) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions,
(iii) "BACE1" (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BACE1" encoded by a nucleic acid that hybridizes to the "BACE1" nucleic acid or its complement under low stringency conditions,
(iv) "DNAJC3" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNAJC3" encoded by a nucleic acid that hybridizes to the "DNAJC3" nucleic acid or its complement under low stringency conditions,
(v) "Neurotrypsin" (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin"

encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,

(vi) "PC7" (SEQ ID No:130) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PC7" encoded by a nucleic acid that hybridizes to the "PC7" nucleic acid or its complement under low stringency conditions,

(vii) "PTPN1" (SEQ ID No:131) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PTPN1" encoded by a nucleic acid that hybridizes to the "PTPN1" nucleic acid or its complement under low stringency conditions, and/or(viii) "Protocadherin beta 7 " (SEQ ID No:132) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 7 " encoded by a nucleic acid that hybridizes to the "Protocadherin beta 7 " nucleic acid or its complement under low stringency conditions,as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders; .

The invention further relates to the following embodiments of the VTRP-complex

1. A protein complex selected from complex (I) and comprising

(a) at least one first protein selected from the group consisting of:

(i) "BET1" (SEQ ID No:137) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BET1" encoded by a nucleic acid that hybridizes to the "BET1" nucleic acid or its complement under low stringency conditions,

(ii) "SYNTAXIN 18" (SEQ ID No:151) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SYNTAXIN 18" encoded by a nucleic acid that hybridizes to the "SYNTAXIN 18" nucleic acid or its complement under low stringency conditions,

(iii) "SYNTAXIN 5" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SYNTAXIN 5"

encoded by a nucleic acid that hybridizes to the "SYNTAXIN 5" nucleic acid or its complement under low stringency conditions, and

(iv) "VTRP" (SEQ ID No:155) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VTRP" encoded by a nucleic acid that hybridizes to the "VTRP" nucleic acid or its complement under low stringency conditions, and

(b) at least one second protein, which second protein is selected from the group consisting of:

(i) "27 KDA GOLGI SNARE PROTEIN" (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "27 KDA GOLGI SNARE PROTEIN" encoded by a nucleic acid that hybridizes to the "27 KDA GOLGI SNARE PROTEIN" nucleic acid or its complement under low stringency conditions,

(ii) "ALPHA-SOLUBLE NSF ATTACHMENT PROTEIN" (SEQ ID No:134) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ALPHA-SOLUBLE NSF ATTACHMENT PROTEIN" encoded by a nucleic acid that hybridizes to the "ALPHA-SOLUBLE NSF ATTACHMENT PROTEIN" nucleic acid or its complement under low stringency conditions,

(iii) "AMYLOID BETA A4 PRECURSOR PROTEIN-BINDING FAMILY B MEMBER 1" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "AMYLOID BETA A4 PRECURSOR PROTEIN-BINDING FAMILY B MEMBER 1" encoded by a nucleic acid that hybridizes to the "AMYLOID BETA A4 PRECURSOR PROTEIN-BINDING FAMILY B MEMBER 1" nucleic acid or its complement under low stringency conditions,

(iv) "BCL2/ADENOVIRUS E1B 19KD-INTERACTING PROTEIN 1, ISOFORM BNIP1" (SEQ ID No:136) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BCL2/ADENOVIRUS E1B 19KD-INTERACTING PROTEIN 1, ISOFORM BNIP1" encoded by a nucleic acid that hybridizes to the "BCL2/ADENOVIRUS E1B 19KD-INTERACTING PROTEIN 1, ISOFORM BNIP1" nucleic acid or its complement under low stringency conditions,

(v) "CALPAIN SMALL SUBUNIT" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CALPAIN SMALL SUBUNIT" encoded by a nucleic acid that hybridizes to the "CALPAIN SMALL SUBUNIT" nucleic acid or its complement under low stringency conditions,

- (vi) "CENTROMERE/KINETOCHORE PROTEIN ZW10 HOMOLOG" (SEQ ID No:139) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CENTROMERE/KINETOCHORE PROTEIN ZW10 HOMOLOG" encoded by a nucleic acid that hybridizes to the "CENTROMERE/KINETOCHORE PROTEIN ZW10 HOMOLOG" nucleic acid or its complement under low stringency conditions,
- (vii) "DYNACTIN COMPLEX 50 KDA SUBUNIT" (SEQ ID No:140) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DYNACTIN COMPLEX 50 KDA SUBUNIT" encoded by a nucleic acid that hybridizes to the "DYNACTIN COMPLEX 50 KDA SUBUNIT" nucleic acid or its complement under low stringency conditions,
- (viii) "GP25L2 PROTEIN" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GP25L2 PROTEIN" encoded by a nucleic acid that hybridizes to the "GP25L2 PROTEIN" nucleic acid or its complement under low stringency conditions,
- (ix) "HSPC009" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC009" encoded by a nucleic acid that hybridizes to the "HSPC009" nucleic acid or its complement under low stringency conditions,
- (x) "HYPOTH 61.5 KDA PROTEIN (FRAGMENT)" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTH 61.5 KDA PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "HYPOTH 61.5 KDA PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xi) "HYPOTH 78.2 KDA PROTEIN (FRAGMENT)" (SEQ ID No:144) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTH 78.2 KDA PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "HYPOTH 78.2 KDA PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xii) "MDS032, UNCHARACTERIZED HEMATOPOIETIC STEM/PROGENITOR CELLS PROTEIN" (SEQ ID No:145) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MDS032, UNCHARACTERIZED HEMATOPOIETIC STEM/PROGENITOR CELLS PROTEIN" encoded by a nucleic acid that hybridizes to the "MDS032, UNCHARACTERIZED

HEMATOPOIETIC STEM/PROGENITOR CELLS PROTEIN" nucleic acid or its complement under low stringency conditions,

(xiii) "NEUROBLASTOMA-AMPLIFIED PROTEIN" (SEQ ID No:146) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEUROBLASTOMA-AMPLIFIED PROTEIN" encoded by a nucleic acid that hybridizes to the "NEUROBLASTOMA-AMPLIFIED PROTEIN" nucleic acid or its complement under low stringency conditions,

(xiv) "Phosphatidylserine receptor" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Phosphatidylserine receptor" encoded by a nucleic acid that hybridizes to the "Phosphatidylserine receptor" nucleic acid or its complement under low stringency conditions,

(xv) "RAD50-INTERACTING PROTEIN 1" (SEQ ID No:148) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAD50-INTERACTING PROTEIN 1" encoded by a nucleic acid that hybridizes to the "RAD50-INTERACTING PROTEIN 1" nucleic acid or its complement under low stringency conditions,

(xvi) "SEC22B VESICLE TRAFFICKING PROTEIN" (SEQ ID No:149) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SEC22B VESICLE TRAFFICKING PROTEIN" encoded by a nucleic acid that hybridizes to the "SEC22B VESICLE TRAFFICKING PROTEIN" nucleic acid or its complement under low stringency conditions,

(xvii) "SYNTAXIN 10" (SEQ ID No:150) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SYNTAXIN 10" encoded by a nucleic acid that hybridizes to the "SYNTAXIN 10" nucleic acid or its complement under low stringency conditions,

(xviii) "Similar to golgi SNAP receptor complex member 1" (SEQ ID No:153) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to golgi SNAP receptor complex member 1" encoded by a nucleic acid that hybridizes to the "Similar to golgi SNAP receptor complex member 1" nucleic acid or its complement under low stringency conditions,

(xix) "Vesicular fusion protein - NSFS" (SEQ ID No:154) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Vesicular fusion protein - NSF" encoded by a nucleic acid that hybridizes to the

"Vesicular fusion protein - NSF" nucleic acid or its complement under low stringency conditions,

and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

2. The protein complex according to No. 1 wherein the first protein is the protein VTRP (SEQ ID NO. 155), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of 'VTRP' encoded by a nucleic acid that hybridizes to the 'VTRP' under low stringency conditions.

3. The protein complex according to No. 1 selected from complex (I) and comprising the following proteins:

- (i) "27 KDA GOLGI SNARE PROTEIN" (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "27 KDA GOLGI SNARE PROTEIN" encoded by a nucleic acid that hybridizes to the "27 KDA GOLGI SNARE PROTEIN" nucleic acid or its complement under low stringency conditions,
- (ii) "ALPHA-SOLUBLE NSF ATTACHMENT PROTEIN" (SEQ ID No:134) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ALPHA-SOLUBLE NSF ATTACHMENT PROTEIN" encoded by a nucleic acid that hybridizes to the "ALPHA-SOLUBLE NSF ATTACHMENT PROTEIN" nucleic acid or its complement under low stringency conditions,
- (iii) "AMYLOID BETA A4 PRECURSOR PROTEIN-BINDING FAMILY B MEMBER 1" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "AMYLOID BETA A4 PRECURSOR PROTEIN-BINDING FAMILY B MEMBER 1" encoded by a nucleic acid that hybridizes to the "AMYLOID BETA A4 PRECURSOR PROTEIN-BINDING FAMILY B MEMBER 1" nucleic acid or its complement under low stringency conditions,

- (iv) "BCL2/ADENOVIRUS E1B 19KD-INTERACTING PROTEIN 1, ISOFORM BNIP1" (SEQ ID No:136) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BCL2/ADENOVIRUS E1B 19KD-INTERACTING PROTEIN 1, ISOFORM BNIP1" encoded by a nucleic acid that hybridizes to the "BCL2/ADENOVIRUS E1B 19KD-INTERACTING PROTEIN 1, ISOFORM BNIP1" nucleic acid or its complement under low stringency conditions,
- (v) "BET1" (SEQ ID No:137) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BET1" encoded by a nucleic acid that hybridizes to the "BET1" nucleic acid or its complement under low stringency conditions,
- (vi) "CALPAIN SMALL SUBUNIT" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CALPAIN SMALL SUBUNIT" encoded by a nucleic acid that hybridizes to the "CALPAIN SMALL SUBUNIT" nucleic acid or its complement under low stringency conditions,
- (vii) "CENTROMERE/KINETOCHEM PROTEIN ZW10 HOMOLOG" (SEQ ID No:139) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CENTROMERE/KINETOCHEM PROTEIN ZW10 HOMOLOG" encoded by a nucleic acid that hybridizes to the "CENTROMERE/KINETOCHEM PROTEIN ZW10 HOMOLOG" nucleic acid or its complement under low stringency conditions,
- (viii) "DYNACTIN COMPLEX 50 KDA SUBUNIT" (SEQ ID No:140) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DYNACTIN COMPLEX 50 KDA SUBUNIT" encoded by a nucleic acid that hybridizes to the "DYNACTIN COMPLEX 50 KDA SUBUNIT" nucleic acid or its complement under low stringency conditions,
- (ix) "GP25L2 PROTEIN" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GP25L2 PROTEIN" encoded by a nucleic acid that hybridizes to the "GP25L2 PROTEIN" nucleic acid or its complement under low stringency conditions,
- (x) "HSPC009" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC009" encoded by a nucleic acid that hybridizes to the "HSPC009" nucleic acid or its complement under low stringency conditions,

- (xi) "HYPOTH 61.5 KDA PROTEIN (FRAGMENT)" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTH 61.5 KDA PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "HYPOTH 61.5 KDA PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xii) "HYPOTH 78.2 KDA PROTEIN (FRAGMENT)" (SEQ ID No:144) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTH 78.2 KDA PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "HYPOTH 78.2 KDA PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xiii) "MDS032, UNCHARACTERIZED HEMATOPOIETIC STEM/PROGENITOR CELLS PROTEIN" (SEQ ID No:145) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MDS032, UNCHARACTERIZED HEMATOPOIETIC STEM/PROGENITOR CELLS PROTEIN" encoded by a nucleic acid that hybridizes to the "MDS032, UNCHARACTERIZED HEMATOPOIETIC STEM/PROGENITOR CELLS PROTEIN" nucleic acid or its complement under low stringency conditions,
- (xiv) "NEUROBLASTOMA-AMPLIFIED PROTEIN" (SEQ ID No:146) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEUROBLASTOMA-AMPLIFIED PROTEIN" encoded by a nucleic acid that hybridizes to the "NEUROBLASTOMA-AMPLIFIED PROTEIN" nucleic acid or its complement under low stringency conditions,
- (xv) "Phosphatidylserine receptor" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Phosphatidylserine receptor" encoded by a nucleic acid that hybridizes to the "Phosphatidylserine receptor" nucleic acid or its complement under low stringency conditions,
- (xvi) "RAD50-INTERACTING PROTEIN 1" (SEQ ID No:148) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAD50-INTERACTING PROTEIN 1" encoded by a nucleic acid that hybridizes to the "RAD50-INTERACTING PROTEIN 1" nucleic acid or its complement under low stringency conditions,
- (xvii) "SEC22B VESICLE TRAFFICKING PROTEIN" (SEQ ID No:149) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof,

or a variant of "SEC22B VESICLE TRAFFICKING PROTEIN" encoded by a nucleic acid that hybridizes to the "SEC22B VESICLE TRAFFICKING PROTEIN" nucleic acid or its complement under low stringency conditions,

(xviii) "SYNTAXIN 10" (SEQ ID No:150) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SYNTAXIN 10" encoded by a nucleic acid that hybridizes to the "SYNTAXIN 10" nucleic acid or its complement under low stringency conditions,

(xix) "SYNTAXIN 18" (SEQ ID No:151) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SYNTAXIN 18" encoded by a nucleic acid that hybridizes to the "SYNTAXIN 18" nucleic acid or its complement under low stringency conditions,

(xx) "SYNTAXIN 5" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SYNTAXIN 5" encoded by a nucleic acid that hybridizes to the "SYNTAXIN 5" nucleic acid or its complement under low stringency conditions,

(xxi) "Similar to golgi SNAP receptor complex member 1" (SEQ ID No:153) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to golgi SNAP receptor complex member 1" encoded by a nucleic acid that hybridizes to the "Similar to golgi SNAP receptor complex member 1" nucleic acid or its complement under low stringency conditions,

(xxii) "VESICULAR-FUSION PROTEIN NSF" (SEQ ID No:154) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VESICULAR-FUSION PROTEIN NSF" encoded by a nucleic acid that hybridizes to the "VESICULAR-FUSION PROTEIN NSF" nucleic acid or its complement under low stringency conditions, and/or

(xxiii) "VTRP" (SEQ ID No:155) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VTRP" encoded by a nucleic acid that hybridizes to the "VTRP" nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 17 of the following proteins:

(i) "27 KDA GOLGI SNARE PROTEIN" (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a

variant of "27 KDA GOLGI SNARE PROTEIN" encoded by a nucleic acid that hybridizes to the "27 KDA GOLGI SNARE PROTEIN" nucleic acid or its complement under low stringency conditions,

- (ii) "ALPHA-SOLUBLE NSF ATTACHMENT PROTEIN" (SEQ ID No:134) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ALPHA-SOLUBLE NSF ATTACHMENT PROTEIN" encoded by a nucleic acid that hybridizes to the "ALPHA-SOLUBLE NSF ATTACHMENT PROTEIN" nucleic acid or its complement under low stringency conditions,
- (iii) "AMYLOID BETA A4 PRECURSOR PROTEIN-BINDING FAMILY B MEMBER 1" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "AMYLOID BETA A4 PRECURSOR PROTEIN-BINDING FAMILY B MEMBER 1" encoded by a nucleic acid that hybridizes to the "AMYLOID BETA A4 PRECURSOR PROTEIN-BINDING FAMILY B MEMBER 1" nucleic acid or its complement under low stringency conditions,
- (iv) "BCL2/ADENOVIRUS E1B 19KD-INTERACTING PROTEIN 1, ISOFORM BNIP1" (SEQ ID No:136) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BCL2/ADENOVIRUS E1B 19KD-INTERACTING PROTEIN 1, ISOFORM BNIP1" encoded by a nucleic acid that hybridizes to the "BCL2/ADENOVIRUS E1B 19KD-INTERACTING PROTEIN 1, ISOFORM BNIP1" nucleic acid or its complement under low stringency conditions,
- (v) "BET1" (SEQ ID No:137) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BET1" encoded by a nucleic acid that hybridizes to the "BET1" nucleic acid or its complement under low stringency conditions,
- (vi) "CALPAIN SMALL SUBUNIT" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CALPAIN SMALL SUBUNIT" encoded by a nucleic acid that hybridizes to the "CALPAIN SMALL SUBUNIT" nucleic acid or its complement under low stringency conditions,
- (vii) "CENTROMERE/KINETOCHEMRE PROTEIN ZW10 HOMOLOG" (SEQ ID No:139) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CENTROMERE/KINETOCHEMRE PROTEIN ZW10 HOMOLOG" encoded by a nucleic acid that hybridizes to the "CENTROMERE/KINETOCHEMRE PROTEIN ZW10 HOMOLOG" nucleic acid or its complement under low stringency conditions,

- (viii) "DYNACTIN COMPLEX 50 KDA SUBUNIT" (SEQ ID No:140) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DYNACTIN COMPLEX 50 KDA SUBUNIT" encoded by a nucleic acid that hybridizes to the "DYNACTIN COMPLEX 50 KDA SUBUNIT" nucleic acid or its complement under low stringency conditions,
- (ix) "GP25L2 PROTEIN" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GP25L2 PROTEIN" encoded by a nucleic acid that hybridizes to the "GP25L2 PROTEIN" nucleic acid or its complement under low stringency conditions,
- (x) "HSPC009" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC009" encoded by a nucleic acid that hybridizes to the "HSPC009" nucleic acid or its complement under low stringency conditions,
- (xi) "HYPOTH 61.5 KDA PROTEIN (FRAGMENT)" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTH 61.5 KDA PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "HYPOTH 61.5 KDA PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xii) "HYPOTH 78.2 KDA PROTEIN (FRAGMENT)" (SEQ ID No:144) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTH 78.2 KDA PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "HYPOTH 78.2 KDA PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xiii) "MDS032, UNCHARACTERIZED HEMATOPOIETIC STEM/PROGENITOR CELLS PROTEIN" (SEQ ID No:145) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MDS032, UNCHARACTERIZED HEMATOPOIETIC STEM/PROGENITOR CELLS PROTEIN" encoded by a nucleic acid that hybridizes to the "MDS032, UNCHARACTERIZED HEMATOPOIETIC STEM/PROGENITOR CELLS PROTEIN" nucleic acid or its complement under low stringency conditions,
- (xiv) "NEUROBLASTOMA-AMPLIFIED PROTEIN" (SEQ ID No:146) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEUROBLASTOMA-AMPLIFIED PROTEIN" encoded by a nucleic acid

that hybridizes to the "NEUROBLASTOMA-AMPLIFIED PROTEIN" nucleic acid or its complement under low stringency conditions,

(xv) "Phosphatidylserine receptor" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Phosphatidylserine receptor" encoded by a nucleic acid that hybridizes to the "Phosphatidylserine receptor" nucleic acid or its complement under low stringency conditions,

(xvi) "RAD50-INTERACTING PROTEIN 1" (SEQ ID No:148) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAD50-INTERACTING PROTEIN 1" encoded by a nucleic acid that hybridizes to the "RAD50-INTERACTING PROTEIN 1" nucleic acid or its complement under low stringency conditions,

(xvii) "SEC22B VESICLE TRAFFICKING PROTEIN" (SEQ ID No:149) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SEC22B VESICLE TRAFFICKING PROTEIN" encoded by a nucleic acid that hybridizes to the "SEC22B VESICLE TRAFFICKING PROTEIN" nucleic acid or its complement under low stringency conditions,

(xviii) "SYNTAXIN 10" (SEQ ID No:150) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SYNTAXIN 10" encoded by a nucleic acid that hybridizes to the "SYNTAXIN 10" nucleic acid or its complement under low stringency conditions,

(xix) "SYNTAXIN 18" (SEQ ID No:151) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SYNTAXIN 18" encoded by a nucleic acid that hybridizes to the "SYNTAXIN 18" nucleic acid or its complement under low stringency conditions,

(xx) "SYNTAXIN 5" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SYNTAXIN 5" encoded by a nucleic acid that hybridizes to the "SYNTAXIN 5" nucleic acid or its complement under low stringency conditions,

(xxi) "Similar to golgi SNAP receptor complex member 1" (SEQ ID No:153) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to golgi SNAP receptor complex member 1" encoded by a nucleic acid that hybridizes to the "Similar to golgi SNAP receptor complex member 1" nucleic acid or its complement under low stringency conditions,

- (xxii) "VESICULAR-FUSION PROTEIN NSF" (SEQ ID No:154) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VESICULAR-FUSION PROTEIN NSF" encoded by a nucleic acid that hybridizes to the "VESICULAR-FUSION PROTEIN NSF" nucleic acid or its complement under low stringency conditions,
- (xxiii) "VTRP" (SEQ ID No:155) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VTRP" encoded by a nucleic acid that hybridizes to the "VTRP" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.

6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.

7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.

8. The complex of any of No. 1 - 7 that is involved in the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by

modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).

9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps: expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.

10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.

11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.

12. Component of the VTRP complex obtainable by a process according to any of No. 9 - 11.

13. Protein of the VTRP complex selected from

(i) "HSPC009" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC009" encoded by a nucleic acid that hybridizes to the "HSPC009" nucleic acid or its complement under low stringency conditions,

(ii) "HYPOTH 61.5 KDA PROTEIN (FRAGMENT)" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTH 61.5 KDA PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "HYPOTH 61.5 KDA PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(iii) "HYPOTH 78.2 KDA PROTEIN (FRAGMENT)" (SEQ ID No:144) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTH 78.2 KDA PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "HYPOTH 78.2 KDA PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(iv) "MDS032, UNCHARACTERIZED HEMATOPOIETIC STEM/PROGENITOR CELLS PROTEIN" (SEQ ID No:145) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MDS032, UNCHARACTERIZED HEMATOPOIETIC STEM/PROGENITOR CELLS PROTEIN" encoded by a nucleic acid that hybridizes to the "MDS032, UNCHARACTERIZED HEMATOPOIETIC STEM/PROGENITOR CELLS PROTEIN" nucleic acid or its complement under low stringency conditions, and

(v) "NEUROBLASTOMA-AMPLIFIED PROTEIN" (SEQ ID No:146) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEUROBLASTOMA-AMPLIFIED PROTEIN" encoded by a nucleic acid that hybridizes to the "NEUROBLASTOMA-AMPLIFIED PROTEIN" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

14. Nucleic acid encoding a protein according to No. 13.

15. Construct, preferably a vector construct, comprising (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or

(b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).

16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the

nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).

17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.
18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.
19. The kit according to No. 18 for processing a substrate of said complex.
20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative disease such as Alzheimer's disease;.
21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.
22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.
23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:
 - (i) "HSPC009" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC009"

encoded by a nucleic acid that hybridizes to the "HSPC009" nucleic acid or its complement under low stringency conditions,

(ii) "HYPOTH 61.5 KDA PROTEIN (FRAGMENT)" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTH 61.5 KDA PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "HYPOTH 61.5 KDA PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(iii) "HYPOTH 78.2 KDA PROTEIN (FRAGMENT)" (SEQ ID No:144) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTH 78.2 KDA PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "HYPOTH 78.2 KDA PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(iv) "MDS032, UNCHARACTERIZED HEMATOPOIETIC STEM/PROGENITOR CELLS PROTEIN" (SEQ ID No:145) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MDS032, UNCHARACTERIZED HEMATOPOIETIC STEM/PROGENITOR CELLS PROTEIN" encoded by a nucleic acid that hybridizes to the "MDS032, UNCHARACTERIZED HEMATOPOIETIC STEM/PROGENITOR CELLS PROTEIN" nucleic acid or its complement under low stringency conditions, and/or

(v) "NEUROBLASTOMA-AMPLIFIED PROTEIN" (SEQ ID No:146) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEUROBLASTOMA-AMPLIFIED PROTEIN" encoded by a nucleic acid that hybridizes to the "NEUROBLASTOMA-AMPLIFIED PROTEIN" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative disease such as Alzheimer's disease;.

25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:

(i) "HSPC009" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC009"

encoded by a nucleic acid that hybridizes to the "HSPC009" nucleic acid or its complement under low stringency conditions,

(ii) "HYPOTH 61.5 KDA PROTEIN (FRAGMENT)" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTH 61.5 KDA PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "HYPOTH 61.5 KDA PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(iii) "HYPOTH 78.2 KDA PROTEIN (FRAGMENT)" (SEQ ID No:144) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTH 78.2 KDA PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "HYPOTH 78.2 KDA PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(iv) "MDS032, UNCHARACTERIZED HEMATOPOIETIC STEM/PROGENITOR CELLS PROTEIN" (SEQ ID No:145) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MDS032, UNCHARACTERIZED HEMATOPOIETIC STEM/PROGENITOR CELLS PROTEIN" encoded by a nucleic acid that hybridizes to the "MDS032, UNCHARACTERIZED HEMATOPOIETIC STEM/PROGENITOR CELLS PROTEIN" nucleic acid or its complement under low stringency conditions, and/or

(v) "NEUROBLASTOMA-AMPLIFIED PROTEIN" (SEQ ID No:146) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEUROBLASTOMA-AMPLIFIED PROTEIN" encoded by a nucleic acid that hybridizes to the "NEUROBLASTOMA-AMPLIFIED PROTEIN" nucleic acid or its complement under low stringency conditions, comprising the steps of

(a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and

(b) determining whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of (a) exposing said complex, or a cell or organism containing VTRP complex to one or more candidate molecules; and

(b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.

28. The method of No. 26, wherein the activity of said complex is determined.

29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.

30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.

31. The method of No. 30, wherein said determining step comprises determining whether

(i) "27 KDA GOLGI SNARE PROTEIN" (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "27 KDA GOLGI SNARE PROTEIN" encoded by a nucleic acid that hybridizes to the "27 KDA GOLGI SNARE PROTEIN" nucleic acid or its complement under low stringency conditions, and/or

(ii) "ALPHA-SOLUBLE NSF ATTACHMENT PROTEIN" (SEQ ID No:134) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ALPHA-SOLUBLE NSF ATTACHMENT PROTEIN"

encoded by a nucleic acid that hybridizes to the "ALPHA-SOLUBLE NSF ATTACHMENT PROTEIN" nucleic acid or its complement under low stringency conditions, and/or

(iii) "AMYLOID BETA A4 PRECURSOR PROTEIN-BINDING FAMILY B MEMBER 1"

(SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "AMYLOID BETA A4

PRECURSOR PROTEIN-BINDING FAMILY B MEMBER 1" encoded by a nucleic acid that hybridizes to the "AMYLOID BETA A4 PRECURSOR PROTEIN-BINDING FAMILY B MEMBER 1" nucleic acid or its complement under low stringency conditions, and/or

(iv) "BCL2/ADENOVIRUS E1B 19KD-INTERACTING PROTEIN 1, ISOFORM BNIP1"

(SEQ ID No:136) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BCL2/ADENOVIRUS E1B 19KD-

INTERACTING PROTEIN 1, ISOFORM BNIP1" encoded by a nucleic acid that

hybridizes to the "BCL2/ADENOVIRUS E1B 19KD-INTERACTING PROTEIN 1, ISOFORM BNIP1" nucleic acid or its complement under low stringency conditions,

and/or

(v) "BET1" (SEQ ID No:137) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BET1" encoded by a nucleic acid that hybridizes to the "BET1" nucleic acid or its complement under low stringency conditions, and/or

(vi) "CALPAIN SMALL SUBUNIT" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"CALPAIN SMALL SUBUNIT" encoded by a nucleic acid that hybridizes to the "CALPAIN SMALL SUBUNIT" nucleic acid or its complement under low stringency conditions, and/or

(vii) "CENTROMERE/KINETOCHEORE PROTEIN ZW10 HOMOLOG" (SEQ ID No:139) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CENTROMERE/KINETOCHEORE PROTEIN ZW10 HOMOLOG" encoded by a nucleic acid that hybridizes to the "CENTROMERE/KINETOCHEORE PROTEIN ZW10 HOMOLOG" nucleic acid or its complement under low stringency conditions, and/or

(viii) "DYNACTIN COMPLEX 50 KDA SUBUNIT" (SEQ ID No:140) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DYNACTIN COMPLEX 50 KDA SUBUNIT" encoded by a nucleic acid

that hybridizes to the "DYNACTIN COMPLEX 50 KDA SUBUNIT" nucleic acid or its complement under low stringency conditions, and/or

(ix) "GP25L2 PROTEIN" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GP25L2 PROTEIN" encoded by a nucleic acid that hybridizes to the "GP25L2 PROTEIN" nucleic acid or its complement under low stringency conditions, and/or

(x) "HSPC009" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC009" encoded by a nucleic acid that hybridizes to the "HSPC009" nucleic acid or its complement under low stringency conditions, and/or

(xi) "HYPOTH 61.5 KDA PROTEIN (FRAGMENT)" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTH 61.5 KDA PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "HYPOTH 61.5 KDA PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or

(xii) "HYPOTH 78.2 KDA PROTEIN (FRAGMENT)" (SEQ ID No:144) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTH 78.2 KDA PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "HYPOTH 78.2 KDA PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or

(xiii) "MDS032, UNCHARACTERIZED HEMATOPOIETIC STEM/PROGENITOR CELLS PROTEIN" (SEQ ID No:145) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MDS032, UNCHARACTERIZED HEMATOPOIETIC STEM/PROGENITOR CELLS PROTEIN" encoded by a nucleic acid that hybridizes to the "MDS032, UNCHARACTERIZED HEMATOPOIETIC STEM/PROGENITOR CELLS PROTEIN" nucleic acid or its complement under low stringency conditions, and/or

(xiv) "NEUROBLASTOMA-AMPLIFIED PROTEIN" (SEQ ID No:146) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEUROBLASTOMA-AMPLIFIED PROTEIN" encoded by a nucleic acid that hybridizes to the "NEUROBLASTOMA-AMPLIFIED PROTEIN" nucleic acid or its complement under low stringency conditions, and/or

(xv) "Phosphatidylserine receptor" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"Phosphatidylserine receptor" encoded by a nucleic acid that hybridizes to the "Phosphatidylserine receptor" nucleic acid or its complement under low stringency conditions, and/or

(xvi) "RAD50-INTERACTING PROTEIN 1" (SEQ ID No:148) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAD50-INTERACTING PROTEIN 1" encoded by a nucleic acid that hybridizes to the "RAD50-INTERACTING PROTEIN 1" nucleic acid or its complement under low stringency conditions, and/or

(xvii) "SEC22B VESICLE TRAFFICKING PROTEIN" (SEQ ID No:149) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SEC22B VESICLE TRAFFICKING PROTEIN" encoded by a nucleic acid that hybridizes to the "SEC22B VESICLE TRAFFICKING PROTEIN" nucleic acid or its complement under low stringency conditions, and/or

(xviii) "SYNTAXIN 10" (SEQ ID No:150) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SYNTAXIN 10" encoded by a nucleic acid that hybridizes to the "SYNTAXIN 10" nucleic acid or its complement under low stringency conditions, and/or

(xix) "SYNTAXIN 18" (SEQ ID No:151) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SYNTAXIN 18" encoded by a nucleic acid that hybridizes to the "SYNTAXIN 18" nucleic acid or its complement under low stringency conditions, and/or

(xx) "SYNTAXIN 5" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SYNTAXIN 5" encoded by a nucleic acid that hybridizes to the "SYNTAXIN 5" nucleic acid or its complement under low stringency conditions, and/or

(xxi) "Similar to golgi SNAP receptor complex member 1" (SEQ ID No:153) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to golgi SNAP receptor complex member 1" encoded by a nucleic acid that hybridizes to the "Similar to golgi SNAP receptor complex member 1" nucleic acid or its complement under low stringency conditions, and/or

(xxii) "VESICULAR-FUSION PROTEIN NSF" (SEQ ID No:154) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VESICULAR-FUSION PROTEIN NSF" encoded by a nucleic acid that

hybridizes to the "VESICULAR-FUSION PROTEIN NSF" nucleic acid or its complement under low stringency conditions, and/or

(xxiii) "VTRP" (SEQ ID No:155) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VTRP" encoded by a nucleic acid that hybridizes to the "VTRP" nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease;;

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease;;

34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.

37. The method of No. 35, wherein the activity of said complex is determined.

38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

40. The method of No. 39, wherein said determining step comprises determining whether
(i) "27 KDA GOLGI SNARE PROTEIN" (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "27 KDA GOLGI SNARE PROTEIN" encoded by a nucleic acid that hybridizes to the "27 KDA GOLGI SNARE PROTEIN" nucleic acid or its complement under low stringency conditions, and/or
(ii) "ALPHA-SOLUBLE NSF ATTACHMENT PROTEIN" (SEQ ID No:134) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ALPHA-SOLUBLE NSF ATTACHMENT PROTEIN" encoded by a nucleic acid that hybridizes to the "ALPHA-SOLUBLE NSF ATTACHMENT PROTEIN" nucleic acid or its complement under low stringency conditions, and/or
(iii) "AMYLOID BETA A4 PRECURSOR PROTEIN-BINDING FAMILY B MEMBER 1" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "AMYLOID BETA A4 PRECURSOR PROTEIN-BINDING FAMILY B MEMBER 1" encoded by a nucleic acid that hybridizes to the "AMYLOID BETA A4 PRECURSOR PROTEIN-BINDING FAMILY B MEMBER 1" nucleic acid or its complement under low stringency conditions, and/or
(iv) "BCL2/ADENOVIRUS E1B 19KD-INTERACTING PROTEIN 1, ISOFORM BNIP1" (SEQ ID No:136) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BCL2/ADENOVIRUS E1B 19KD-

INTERACTING PROTEIN 1, ISOFORM BNIP1" encoded by a nucleic acid that hybridizes to the "BCL2/ADENOVIRUS E1B 19KD-INTERACTING PROTEIN 1, ISOFORM BNIP1" nucleic acid or its complement under low stringency conditions, and/or

- (v) "BET1" (SEQ ID No:137) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BET1" encoded by a nucleic acid that hybridizes to the "BET1" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "CALPAIN SMALL SUBUNIT" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CALPAIN SMALL SUBUNIT" encoded by a nucleic acid that hybridizes to the "CALPAIN SMALL SUBUNIT" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "CENTROMERE/KINETOCHEMRE PROTEIN ZW10 HOMOLOG" (SEQ ID No:139) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CENTROMERE/KINETOCHEMRE PROTEIN ZW10 HOMOLOG" encoded by a nucleic acid that hybridizes to the "CENTROMERE/KINETOCHEMRE PROTEIN ZW10 HOMOLOG" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "DYNACTIN COMPLEX 50 KDA SUBUNIT" (SEQ ID No:140) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DYNACTIN COMPLEX 50 KDA SUBUNIT" encoded by a nucleic acid that hybridizes to the "DYNACTIN COMPLEX 50 KDA SUBUNIT" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "GP25L2 PROTEIN" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GP25L2 PROTEIN" encoded by a nucleic acid that hybridizes to the "GP25L2 PROTEIN" nucleic acid or its complement under low stringency conditions, and/or
- (x) "HSPC009" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC009" encoded by a nucleic acid that hybridizes to the "HSPC009" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "HYPOTH 61.5 KDA PROTEIN (FRAGMENT)" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof,

or a variant of "HYPOTH 61.5 KDA PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "HYPOTH 61.5 KDA PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or

(xii) "HYPOTH 78.2 KDA PROTEIN (FRAGMENT)" (SEQ ID No:144) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTH 78.2 KDA PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "HYPOTH 78.2 KDA PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or

(xiii) "MDS032, UNCHARACTERIZED HEMATOPOIETIC STEM/PROGENITOR CELLS PROTEIN" (SEQ ID No:145) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MDS032, UNCHARACTERIZED HEMATOPOIETIC STEM/PROGENITOR CELLS PROTEIN" encoded by a nucleic acid that hybridizes to the "MDS032, UNCHARACTERIZED HEMATOPOIETIC STEM/PROGENITOR CELLS PROTEIN" nucleic acid or its complement under low stringency conditions, and/or

(xiv) "NEUROBLASTOMA-AMPLIFIED PROTEIN" (SEQ ID No:146) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEUROBLASTOMA-AMPLIFIED PROTEIN" encoded by a nucleic acid that hybridizes to the "NEUROBLASTOMA-AMPLIFIED PROTEIN" nucleic acid or its complement under low stringency conditions, and/or

(xv) "Phosphatidylserine receptor" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Phosphatidylserine receptor" encoded by a nucleic acid that hybridizes to the "Phosphatidylserine receptor" nucleic acid or its complement under low stringency conditions, and/or

(xvi) "RAD50-INTERACTING PROTEIN 1" (SEQ ID No:148) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAD50-INTERACTING PROTEIN 1" encoded by a nucleic acid that hybridizes to the "RAD50-INTERACTING PROTEIN 1" nucleic acid or its complement under low stringency conditions, and/or

(xvii) "SEC22B VESICLE TRAFFICKING PROTEIN" (SEQ ID No:149) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SEC22B VESICLE TRAFFICKING PROTEIN" encoded by a nucleic acid

that hybridizes to the "SEC22B VESICLE TRAFFICKING PROTEIN" nucleic acid or its complement under low stringency conditions, and/or

(xviii) "SYNTAXIN 10" (SEQ ID No:150) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SYNTAXIN 10" encoded by a nucleic acid that hybridizes to the "SYNTAXIN 10" nucleic acid or its complement under low stringency conditions, and/or

(xix) "SYNTAXIN 18" (SEQ ID No:151) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SYNTAXIN 18" encoded by a nucleic acid that hybridizes to the "SYNTAXIN 18" nucleic acid or its complement under low stringency conditions, and/or

(xx) "SYNTAXIN 5" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SYNTAXIN 5" encoded by a nucleic acid that hybridizes to the "SYNTAXIN 5" nucleic acid or its complement under low stringency conditions, and/or

(xxi) "Similar to golgi SNAP receptor complex member 1" (SEQ ID No:153) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to golgi SNAP receptor complex member 1" encoded by a nucleic acid that hybridizes to the "Similar to golgi SNAP receptor complex member 1" nucleic acid or its complement under low stringency conditions, and/or

(xxii) "VESICULAR-FUSION PROTEIN NSF" (SEQ ID No:154) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VESICULAR-FUSION PROTEIN NSF" encoded by a nucleic acid that hybridizes to the "VESICULAR-FUSION PROTEIN NSF" nucleic acid or its complement under low stringency conditions, and/or

(xxiii) "VTRP" (SEQ ID No:155) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VTRP" encoded by a nucleic acid that hybridizes to the "VTRP" nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative disease such as Alzheimer's disease;.

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42 , wherein said disease or disorder involves increased levels of the amount or activity of said complex.

45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins
(i) "27 KDA GOLGI SNARE PROTEIN" (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "27 KDA GOLGI SNARE PROTEIN" encoded by a nucleic acid that hybridizes to the "27 KDA GOLGI SNARE PROTEIN" nucleic acid or its complement under low stringency conditions,
(ii) "ALPHA-SOLUBLE NSF ATTACHMENT PROTEIN" (SEQ ID No:134) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ALPHA-SOLUBLE NSF ATTACHMENT PROTEIN" encoded by a nucleic acid that hybridizes to the "ALPHA-SOLUBLE NSF ATTACHMENT PROTEIN" nucleic acid or its complement under low stringency conditions,

- (iii) "AMYLOID BETA A4 PRECURSOR PROTEIN-BINDING FAMILY B MEMBER 1" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "AMYLOID BETA A4 PRECURSOR PROTEIN-BINDING FAMILY B MEMBER 1" encoded by a nucleic acid that hybridizes to the "AMYLOID BETA A4 PRECURSOR PROTEIN-BINDING FAMILY B MEMBER 1" nucleic acid or its complement under low stringency conditions,
- (iv) "BCL2/ADENOVIRUS E1B 19KD-INTERACTING PROTEIN 1, ISOFORM BNIP1" (SEQ ID No:136) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BCL2/ADENOVIRUS E1B 19KD-INTERACTING PROTEIN 1, ISOFORM BNIP1" encoded by a nucleic acid that hybridizes to the "BCL2/ADENOVIRUS E1B 19KD-INTERACTING PROTEIN 1, ISOFORM BNIP1" nucleic acid or its complement under low stringency conditions,
- (v) "BET1" (SEQ ID No:137) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BET1" encoded by a nucleic acid that hybridizes to the "BET1" nucleic acid or its complement under low stringency conditions,
- (vi) "CALPAIN SMALL SUBUNIT" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CALPAIN SMALL SUBUNIT" encoded by a nucleic acid that hybridizes to the "CALPAIN SMALL SUBUNIT" nucleic acid or its complement under low stringency conditions,
- (vii) "CENTROMERE/KINETOCHEMRE PROTEIN ZW10 HOMOLOG" (SEQ ID No:139) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CENTROMERE/KINETOCHEMRE PROTEIN ZW10 HOMOLOG" encoded by a nucleic acid that hybridizes to the "CENTROMERE/KINETOCHEMRE PROTEIN ZW10 HOMOLOG" nucleic acid or its complement under low stringency conditions,
- (viii) "DYNACTIN COMPLEX 50 KDA SUBUNIT" (SEQ ID No:140) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DYNACTIN COMPLEX 50 KDA SUBUNIT" encoded by a nucleic acid that hybridizes to the "DYNACTIN COMPLEX 50 KDA SUBUNIT" nucleic acid or its complement under low stringency conditions,
- (ix) "GP25L2 PROTEIN" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GP25L2

PROTEIN" encoded by a nucleic acid that hybridizes to the "GP25L2 PROTEIN" nucleic acid or its complement under low stringency conditions,

(x) "HSPC009" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC009" encoded by a nucleic acid that hybridizes to the "HSPC009" nucleic acid or its complement under low stringency conditions,

(xi) "HYPOTH 61.5 KDA PROTEIN (FRAGMENT)" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTH 61.5 KDA PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "HYPOTH 61.5 KDA PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xii) "HYPOTH 78.2 KDA PROTEIN (FRAGMENT)" (SEQ ID No:144) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTH 78.2 KDA PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "HYPOTH 78.2 KDA PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xiii) "MDS032, UNCHARACTERIZED HEMATOPOIETIC STEM/PROGENITOR CELLS PROTEIN" (SEQ ID No:145) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MDS032, UNCHARACTERIZED HEMATOPOIETIC STEM/PROGENITOR CELLS PROTEIN" encoded by a nucleic acid that hybridizes to the "MDS032, UNCHARACTERIZED HEMATOPOIETIC STEM/PROGENITOR CELLS PROTEIN" nucleic acid or its complement under low stringency conditions,

(xiv) "NEUROBLASTOMA-AMPLIFIED PROTEIN" (SEQ ID No:146) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEUROBLASTOMA-AMPLIFIED PROTEIN" encoded by a nucleic acid that hybridizes to the "NEUROBLASTOMA-AMPLIFIED PROTEIN" nucleic acid or its complement under low stringency conditions,

(xv) "Phosphatidylserine receptor" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Phosphatidylserine receptor" encoded by a nucleic acid that hybridizes to the "Phosphatidylserine receptor" nucleic acid or its complement under low stringency conditions,

- (xvi) "RAD50-INTERACTING PROTEIN 1" (SEQ ID No:148) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAD50-INTERACTING PROTEIN 1" encoded by a nucleic acid that hybridizes to the "RAD50-INTERACTING PROTEIN 1" nucleic acid or its complement under low stringency conditions,
- (xvii) "SEC22B VESICLE TRAFFICKING PROTEIN" (SEQ ID No:149) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SEC22B VESICLE TRAFFICKING PROTEIN" encoded by a nucleic acid that hybridizes to the "SEC22B VESICLE TRAFFICKING PROTEIN" nucleic acid or its complement under low stringency conditions,
- (xviii) "SYNTAXIN 10" (SEQ ID No:150) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SYNTAXIN 10" encoded by a nucleic acid that hybridizes to the "SYNTAXIN 10" nucleic acid or its complement under low stringency conditions,
- (xix) "SYNTAXIN 18" (SEQ ID No:151) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SYNTAXIN 18" encoded by a nucleic acid that hybridizes to the "SYNTAXIN 18" nucleic acid or its complement under low stringency conditions,
- (xx) "SYNTAXIN 5" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SYNTAXIN 5" encoded by a nucleic acid that hybridizes to the "SYNTAXIN 5" nucleic acid or its complement under low stringency conditions,
- (xxi) "Similar to golgi SNAP receptor complex member 1" (SEQ ID No:153) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to golgi SNAP receptor complex member 1" encoded by a nucleic acid that hybridizes to the "Similar to golgi SNAP receptor complex member 1" nucleic acid or its complement under low stringency conditions,
- (xxii) "VESICULAR-FUSION PROTEIN NSF" (SEQ ID No:154) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VESICULAR-FUSION PROTEIN NSF" encoded by a nucleic acid that hybridizes to the "VESICULAR-FUSION PROTEIN NSF" nucleic acid or its complement under low stringency conditions, and/or(xxiii) "VTRP" (SEQ ID No:155) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VTRP" encoded by a nucleic acid that hybridizes to the "VTRP" nucleic

acid or its complement under low stringency conditions, as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease;.

The invention further relates to the following embodiments of the Bace1-complex

1. A protein complex selected from complex (I) and comprising

(a) at least one first protein selected from the group consisting of:

(i) "BACE1" (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BACE1" encoded by a nucleic acid that hybridizes to the "BACE1" nucleic acid or its complement under low stringency conditions, and

(ii) "Nicastrin" (SEQ ID No:165) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and

(b) at least one second protein, which second protein is selected from the group consisting of:

(i) "CGI-13" (SEQ ID No:156) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,

(ii) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions,

(iii) "Calsyntenin 1" (SEQ ID No:158) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin 1" encoded by a nucleic acid that hybridizes to the "Calsyntenin 1" nucleic acid or its complement under low stringency conditions,

(iv) "Delta-6 fatty acid desaturase " (SEQ ID No:159) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

- "Delta-6 fatty acid desaturase " encoded by a nucleic acid that hybridizes to the "Delta-6 fatty acid desaturase " nucleic acid or its complement under low stringency conditions,
- (v) "Delta-like homolog" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-like homolog" encoded by a nucleic acid that hybridizes to the "Delta-like homolog" nucleic acid or its complement under low stringency conditions,
- (vi) "FLJ30668" (SEQ ID No:161) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ30668" encoded by a nucleic acid that hybridizes to the "FLJ30668" nucleic acid or its complement under low stringency conditions,
- (vii) "FLJ39249" (SEQ ID No:162) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ39249" encoded by a nucleic acid that hybridizes to the "FLJ39249" nucleic acid or its complement under low stringency conditions,
- (viii) "ITCH" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITCH" encoded by a nucleic acid that hybridizes to the "ITCH" nucleic acid or its complement under low stringency conditions,
- (ix) "KIAA1250" (SEQ ID No:164) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions,
- (x) "Nogo-A" (SEQ ID No:166) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nogo-A" encoded by a nucleic acid that hybridizes to the "Nogo-A" nucleic acid or its complement under low stringency conditions,
- (xi) "PDGFRB" (SEQ ID No:167) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDGFRB" encoded by a nucleic acid that hybridizes to the "PDGFRB" nucleic acid or its complement under low stringency conditions,
- (xii) "PTK7" (SEQ ID No:168) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PTK7" encoded by a nucleic acid that hybridizes to the "PTK7" nucleic acid or its complement under low stringency conditions,

- (xiii) "SERPINA1" (SEQ ID No:169) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SERPINA1" encoded by a nucleic acid that hybridizes to the "SERPINA1" nucleic acid or its complement under low stringency conditions,
- (xiv) "SIM TO Y71H10A. 2.P" (SEQ ID No:170) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIM TO Y71H10A. 2.P" encoded by a nucleic acid that hybridizes to the "SIM TO Y71H10A. 2.P" nucleic acid or its complement under low stringency conditions,
- (xv) "STX10" (SEQ ID No:150) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX10" encoded by a nucleic acid that hybridizes to the "STX10" nucleic acid or its complement under low stringency conditions,
- (xvi) "Sortilin-related receptor" (SEQ ID No:171) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin-related receptor" encoded by a nucleic acid that hybridizes to the "Sortilin-related receptor" nucleic acid or its complement under low stringency conditions,
- (xvii) "Thioredoxin domain-containing protein" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,
- (xviii) "integral membrane transporter protein" (SEQ ID No:173) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "integral membrane transporter protein" nucleic acid or its complement under low stringency conditions, and
- (xix) "kinectin 1 (kinesin receptor)" (SEQ ID No:174) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "kinectin 1 (kinesin receptor)" encoded by a nucleic acid that hybridizes to the "kinectin 1 (kinesin receptor)" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40

Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

2. The protein complex according to No. 1 wherein the first protein is the protein Bace1 (SEQ ID NO. 129), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of 'Bace1' encoded by a nucleic acid that hybridizes to the 'Bace1' under low stringency conditions.
3. The protein complex according to No. 1 selected from complex (I) and comprising the following proteins:
 - (i) "BACE1" (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BACE1" encoded by a nucleic acid that hybridizes to the "BACE1" nucleic acid or its complement under low stringency conditions,
 - (ii) "CGI-13" (SEQ ID No:156) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
 - (iii) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions,
 - (iv) "Calsyntenin 1" (SEQ ID No:158) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin 1" encoded by a nucleic acid that hybridizes to the "Calsyntenin 1" nucleic acid or its complement under low stringency conditions,
 - (v) "Delta-6 fatty acid desaturase " (SEQ ID No:159) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-6 fatty acid desaturase " encoded by a nucleic acid that hybridizes to the "Delta-6 fatty acid desaturase " nucleic acid or its complement under low stringency conditions,

- (vi) "Delta-like homolog" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-like homolog" encoded by a nucleic acid that hybridizes to the "Delta-like homolog" nucleic acid or its complement under low stringency conditions,
- (vii) "FLJ30668" (SEQ ID No:161) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ30668" encoded by a nucleic acid that hybridizes to the "FLJ30668" nucleic acid or its complement under low stringency conditions,
- (viii) "FLJ39249" (SEQ ID No:162) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ39249" encoded by a nucleic acid that hybridizes to the "FLJ39249" nucleic acid or its complement under low stringency conditions,
- (ix) "ITCH" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITCH" encoded by a nucleic acid that hybridizes to the "ITCH" nucleic acid or its complement under low stringency conditions,
- (x) "KIAA1250" (SEQ ID No:164) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions,
- (xi) "Nicastrin" (SEQ ID No:165) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,
- (xii) "Nogo-A" (SEQ ID No:166) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nogo-A" encoded by a nucleic acid that hybridizes to the "Nogo-A" nucleic acid or its complement under low stringency conditions,
- (xiii) "PDGFRB" (SEQ ID No:167) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDGFRB" encoded by a nucleic acid that hybridizes to the "PDGFRB" nucleic acid or its complement under low stringency conditions,
- (xiv) "PTK7" (SEQ ID No:168) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PTK7" encoded by a

nucleic acid that hybridizes to the "PTK7" nucleic acid or its complement under low stringency conditions,

(xv) "SERPINA1" (SEQ ID No:169) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SERPINA1" encoded by a nucleic acid that hybridizes to the "SERPINA1" nucleic acid or its complement under low stringency conditions,

(xvi) "SIM TO Y71H10A. 2.P" (SEQ ID No:170) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIM TO Y71H10A. 2.P" encoded by a nucleic acid that hybridizes to the "SIM TO Y71H10A. 2.P" nucleic acid or its complement under low stringency conditions,

(xvii) "STX10" (SEQ ID No:150) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX10" encoded by a nucleic acid that hybridizes to the "STX10" nucleic acid or its complement under low stringency conditions,

(xviii) "Sortilin-related receptor" (SEQ ID No:171) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin-related receptor" encoded by a nucleic acid that hybridizes to the "Sortilin-related receptor" nucleic acid or its complement under low stringency conditions,

(xix) "Thioredoxin domain-containing protein" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,

(xx) "integral membrane transporter protein" (SEQ ID No:173) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "integral membrane transporter protein" nucleic acid or its complement under low stringency conditions, and/or

(xxi) "kinectin 1 (kinesin receptor)" (SEQ ID No:174) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "kinectin 1 (kinesin receptor)" encoded by a nucleic acid that hybridizes to the "kinectin 1 (kinesin receptor)" nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 18 of the following proteins:

- (i) "BACE1" (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BACE1" encoded by a nucleic acid that hybridizes to the "BACE1" nucleic acid or its complement under low stringency conditions,
- (ii) "CGI-13" (SEQ ID No:156) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
- (iii) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions,
- (iv) "Calsyntenin 1" (SEQ ID No:158) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin 1" encoded by a nucleic acid that hybridizes to the "Calsyntenin 1" nucleic acid or its complement under low stringency conditions,
- (v) "Delta-6 fatty acid desaturase " (SEQ ID No:159) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-6 fatty acid desaturase " encoded by a nucleic acid that hybridizes to the "Delta-6 fatty acid desaturase " nucleic acid or its complement under low stringency conditions,
- (vi) "Delta-like homolog" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-like homolog" encoded by a nucleic acid that hybridizes to the "Delta-like homolog" nucleic acid or its complement under low stringency conditions,
- (vii) "FLJ30668" (SEQ ID No:161) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ30668" encoded by a nucleic acid that hybridizes to the "FLJ30668" nucleic acid or its complement under low stringency conditions,
- (viii) "FLJ39249" (SEQ ID No:162) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ39249"

- encoded by a nucleic acid that hybridizes to the "FLJ39249" nucleic acid or its complement under low stringency conditions,
- (ix) "ITCH" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITCH" encoded by a nucleic acid that hybridizes to the "ITCH" nucleic acid or its complement under low stringency conditions,
- (x) "KIAA1250" (SEQ ID No:164) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions,
- (xi) "Nicastrin" (SEQ ID No:165) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,
- (xii) "Nogo-A" (SEQ ID No:166) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nogo-A" encoded by a nucleic acid that hybridizes to the "Nogo-A" nucleic acid or its complement under low stringency conditions,
- (xiii) "PDGFRB" (SEQ ID No:167) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDGFRB" encoded by a nucleic acid that hybridizes to the "PDGFRB" nucleic acid or its complement under low stringency conditions,
- (xiv) "PTK7" (SEQ ID No:168) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PTK7" encoded by a nucleic acid that hybridizes to the "PTK7" nucleic acid or its complement under low stringency conditions,
- (xv) "SERPINA1" (SEQ ID No:169) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SERPINA1" encoded by a nucleic acid that hybridizes to the "SERPINA1" nucleic acid or its complement under low stringency conditions,
- (xvi) "SIM TO Y71H10A. 2.P" (SEQ ID No:170) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIM TO Y71H10A. 2.P" encoded by a nucleic acid that hybridizes to the "SIM TO Y71H10A. 2.P" nucleic acid or its complement under low stringency conditions,

- (xvii) "STX10" (SEQ ID No:150) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX10" encoded by a nucleic acid that hybridizes to the "STX10" nucleic acid or its complement under low stringency conditions,
- (xviii) "Sortilin-related receptor" (SEQ ID No:171) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin-related receptor" encoded by a nucleic acid that hybridizes to the "Sortilin-related receptor" nucleic acid or its complement under low stringency conditions,
- (xix) "Thioredoxin domain-containing protein" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,
- (xx) "integral membrane transporter protein" (SEQ ID No:173) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,
- (xi) "kinectin 1 (kinesin receptor)" (SEQ ID No:174) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "kinectin 1 (kinesin receptor)" encoded by a nucleic acid that hybridizes to the "kinectin 1 (kinesin receptor)" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.

6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.

7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.
8. The complex of any of No. 1 - 7 that is involved in the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).
9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps: expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.
10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.
11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.
12. Component of the BACE1 complex obtainable by a process according to any of No. 9 - 11.
13. Protein of the BACE1 complex selected from

- (i) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions,
- (ii) "FLJ30668" (SEQ ID No:161) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ30668" encoded by a nucleic acid that hybridizes to the "FLJ30668" nucleic acid or its complement under low stringency conditions,
- (iii) "FLJ39249" (SEQ ID No:162) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ39249" encoded by a nucleic acid that hybridizes to the "FLJ39249" nucleic acid or its complement under low stringency conditions,
- (iv) "KIAA1250" (SEQ ID No:164) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions,
- (v) "SIM TO Y71H10A. 2.P" (SEQ ID No:170) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIM TO Y71H10A. 2.P" encoded by a nucleic acid that hybridizes to the "SIM TO Y71H10A. 2.P" nucleic acid or its complement under low stringency conditions, and
- (vi) "Thioredoxin domain-containing protein" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

14. Nucleic acid encoding a protein according to No. 13.

15. Construct, preferably a vector construct, comprising (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or
(b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).
16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).
17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.
18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.
19. The kit according to No. 18 for processing a substrate of said complex.

20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.
21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.
22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.
23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:
- (i) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions,
 - (ii) "FLJ30668" (SEQ ID No:161) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ30668" encoded by a nucleic acid that hybridizes to the "FLJ30668" nucleic acid or its complement under low stringency conditions,
 - (iii) "FLJ39249" (SEQ ID No:162) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ39249" encoded by a nucleic acid that hybridizes to the "FLJ39249" nucleic acid or its complement under low stringency conditions,
 - (iv) "KIAA1250" (SEQ ID No:164) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions,
 - (v) "SIM TO Y71H10A. 2.P" (SEQ ID No:170) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIM TO

Y71H10A. 2.P" encoded by a nucleic acid that hybridizes to the "SIM TO Y71H10A. 2.P" nucleic acid or its complement under low stringency conditions, and/or

(vi) "Thioredoxin domain-containing protein" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:

- (i) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions,
- (ii) "FLJ30668" (SEQ ID No:161) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ30668" encoded by a nucleic acid that hybridizes to the "FLJ30668" nucleic acid or its complement under low stringency conditions,
- (iii) "FLJ39249" (SEQ ID No:162) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ39249" encoded by a nucleic acid that hybridizes to the "FLJ39249" nucleic acid or its complement under low stringency conditions,
- (iv) "KIAA1250" (SEQ ID No:164) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions,

- (v) "SIM TO Y71H10A. 2.P" (SEQ ID No:170) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIM TO Y71H10A. 2.P" encoded by a nucleic acid that hybridizes to the "SIM TO Y71H10A. 2.P" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "Thioredoxin domain-containing protein" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions, comprising the steps of
 - (a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and
 - (b) determining whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of (a) exposing said complex, or a cell or organism containing BACE1 complex to one or more candidate molecules; and

(b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.

28. The method of No. 26, wherein the activity of said complex is determined.

29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.
30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.
31. The method of No. 30, wherein said determining step comprises determining whether
- (i) "BACE1" (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BACE1" encoded by a nucleic acid that hybridizes to the "BACE1" nucleic acid or its complement under low stringency conditions, and/or
 - (ii) "CGI-13" (SEQ ID No:156) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions, and/or
 - (iii) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions, and/or
 - (iv) "Calsyntenin 1" (SEQ ID No:158) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin 1" encoded by a nucleic acid that hybridizes to the "Calsyntenin 1" nucleic acid or its complement under low stringency conditions, and/or
 - (v) "Delta-6 fatty acid desaturase " (SEQ ID No:159) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-6 fatty acid desaturase " encoded by a nucleic acid that hybridizes to the "Delta-6 fatty acid desaturase " nucleic acid or its complement under low stringency conditions, and/or
 - (vi) "Delta-like homolog" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-like

homolog" encoded by a nucleic acid that hybridizes to the "Delta-like homolog" nucleic acid or its complement under low stringency conditions, and/or

(vii) "FLJ30668" (SEQ ID No:161) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ30668" encoded by a nucleic acid that hybridizes to the "FLJ30668" nucleic acid or its complement under low stringency conditions, and/or

(viii) "FLJ39249" (SEQ ID No:162) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ39249" encoded by a nucleic acid that hybridizes to the "FLJ39249" nucleic acid or its complement under low stringency conditions, and/or

(ix) "ITCH" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITCH" encoded by a nucleic acid that hybridizes to the "ITCH" nucleic acid or its complement under low stringency conditions, and/or

(x) "KIAA1250" (SEQ ID No:164) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions, and/or

(xi) "Nicastrin" (SEQ ID No:165) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and/or

(xii) "Nogo-A" (SEQ ID No:166) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nogo-A" encoded by a nucleic acid that hybridizes to the "Nogo-A" nucleic acid or its complement under low stringency conditions, and/or

(xiii) "PDGFRB" (SEQ ID No:167) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDGFRB" encoded by a nucleic acid that hybridizes to the "PDGFRB" nucleic acid or its complement under low stringency conditions, and/or

(xiv) "PTK7" (SEQ ID No:168) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PTK7" encoded by a nucleic acid that hybridizes to the "PTK7" nucleic acid or its complement under low stringency conditions, and/or

- (xv) "SERPINA1" (SEQ ID No:169) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SERPINA1" encoded by a nucleic acid that hybridizes to the "SERPINA1" nucleic acid or its complement under low stringency conditions, and/or
- (xvi) "SIM TO Y71H10A. 2.P" (SEQ ID No:170) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIM TO Y71H10A. 2.P" encoded by a nucleic acid that hybridizes to the "SIM TO Y71H10A. 2.P" nucleic acid or its complement under low stringency conditions, and/or
- (xvii) "STX10" (SEQ ID No:150) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX10" encoded by a nucleic acid that hybridizes to the "STX10" nucleic acid or its complement under low stringency conditions, and/or
- (xviii) "Sortilin-related receptor" (SEQ ID No:171) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin-related receptor" encoded by a nucleic acid that hybridizes to the "Sortilin-related receptor" nucleic acid or its complement under low stringency conditions, and/or
- (xix) "Thioredoxin domain-containing protein" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions, and/or
- (xx) "integral membrane transporter protein" (SEQ ID No:173) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "integral membrane transporter protein" nucleic acid or its complement under low stringency conditions, and/or
- (xxi) "kinectin 1 (kinesin receptor)" (SEQ ID No:174) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "kinectin 1 (kinesin receptor)" encoded by a nucleic acid that hybridizes to the "kinectin 1 (kinesin receptor)" nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.

37. The method of No. 35, wherein the activity of said complex is determined.

38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said

complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

40. The method of No. 39, wherein said determining step comprises determining whether

- (i) "BACE1" (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BACE1" encoded by a nucleic acid that hybridizes to the "BACE1" nucleic acid or its complement under low stringency conditions, and/or
- (ii) "CGI-13" (SEQ ID No:156) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "Calsyntenin 1" (SEQ ID No:158) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin 1" encoded by a nucleic acid that hybridizes to the "Calsyntenin 1" nucleic acid or its complement under low stringency conditions, and/or
- (v) "Delta-6 fatty acid desaturase " (SEQ ID No:159) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-6 fatty acid desaturase " encoded by a nucleic acid that hybridizes to the "Delta-6 fatty acid desaturase " nucleic acid or its complement under low stringency conditions, and/or
- (vi) "Delta-like homolog" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-like homolog" encoded by a nucleic acid that hybridizes to the "Delta-like homolog" nucleic acid or its complement under low stringency conditions, and/or

- (vii) "FLJ30668" (SEQ ID No:161) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ30668" encoded by a nucleic acid that hybridizes to the "FLJ30668" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "FLJ39249" (SEQ ID No:162) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ39249" encoded by a nucleic acid that hybridizes to the "FLJ39249" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "ITCH" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITCH" encoded by a nucleic acid that hybridizes to the "ITCH" nucleic acid or its complement under low stringency conditions, and/or
- (x) "KIAA1250" (SEQ ID No:164) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "Nicastin" (SEQ ID No:165) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastin" encoded by a nucleic acid that hybridizes to the "Nicastin" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "Nogo-A" (SEQ ID No:166) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nogo-A" encoded by a nucleic acid that hybridizes to the "Nogo-A" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "PDGFRB" (SEQ ID No:167) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDGFRB" encoded by a nucleic acid that hybridizes to the "PDGFRB" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "PTK7" (SEQ ID No:168) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PTK7" encoded by a nucleic acid that hybridizes to the "PTK7" nucleic acid or its complement under low stringency conditions, and/or
- (xv) "SERPINA1" (SEQ ID No:169) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SERPINA1"

encoded by a nucleic acid that hybridizes to the "SERPINA1" nucleic acid or its complement under low stringency conditions, and/or
(xvi) "SIM TO Y71H10A. 2.P" (SEQ ID No:170) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIM TO Y71H10A. 2.P" encoded by a nucleic acid that hybridizes to the "SIM TO Y71H10A. 2.P" nucleic acid or its complement under low stringency conditions, and/or
(xvii) "STX10" (SEQ ID No:150) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX10" encoded by a nucleic acid that hybridizes to the "STX10" nucleic acid or its complement under low stringency conditions, and/or
(xviii) "Sortilin-related receptor" (SEQ ID No:171) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin-related receptor" encoded by a nucleic acid that hybridizes to the "Sortilin-related receptor" nucleic acid or its complement under low stringency conditions, and/or
(xix) "Thioredoxin domain-containing protein" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions, and/or
(xx) "integral membrane transporter protein" (SEQ ID No:173) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "integral membrane transporter protein" nucleic acid or its complement under low stringency conditions, and/or
(xxi) "kinectin 1 (kinesin receptor)" (SEQ ID No:174) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "kinectin 1 (kinesin receptor)" encoded by a nucleic acid that hybridizes to the "kinectin 1 (kinesin receptor)" nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as

neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42 , wherein said disease or disorder involves increased levels of the amount or activity of said complex.

45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins
(i) "BACE1" (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BACE1" encoded by a nucleic acid that hybridizes to the "BACE1" nucleic acid or its complement under low stringency conditions,
(ii) "CGI-13" (SEQ ID No:156) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a

nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,

- (iii) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions,
- (iv) "Calsyntenin 1" (SEQ ID No:158) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin 1". encoded by a nucleic acid that hybridizes to the "Calsyntenin 1" nucleic acid or its complement under low stringency conditions,
- (v) "Delta-6 fatty acid desaturase " (SEQ ID No:159) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-6 fatty acid desaturase " encoded by a nucleic acid that hybridizes to the "Delta-6 fatty acid desaturase " nucleic acid or its complement under low stringency conditions,
- (vi) "Delta-like homolog" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-like homolog" encoded by a nucleic acid that hybridizes to the "Delta-like homolog" nucleic acid or its complement under low stringency conditions,
- (vii) "FLJ30668" (SEQ ID No:161) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ30668" encoded by a nucleic acid that hybridizes to the "FLJ30668" nucleic acid or its complement under low stringency conditions,
- (viii) "FLJ39249" (SEQ ID No:162) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ39249" encoded by a nucleic acid that hybridizes to the "FLJ39249" nucleic acid or its complement under low stringency conditions,
- (ix) "ITCH" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITCH" encoded by a nucleic acid that hybridizes to the "ITCH" nucleic acid or its complement under low stringency conditions,
- (x) "KIAA1250" (SEQ ID No:164) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250"

encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions,

(xi) "Nicastrin" (SEQ ID No:165) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicestrin" nucleic acid or its complement under low stringency conditions,

(xii) "Nogo-A" (SEQ ID No:166) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nogo-A" encoded by a nucleic acid that hybridizes to the "Nogo-A" nucleic acid or its complement under low stringency conditions,

(xiii) "PDGFRB" (SEQ ID No:167) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDGFRB" encoded by a nucleic acid that hybridizes to the "PDGFRB" nucleic acid or its complement under low stringency conditions,

(xiv) "PTK7" (SEQ ID No:168) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PTK7" encoded by a nucleic acid that hybridizes to the "PTK7" nucleic acid or its complement under low stringency conditions,

(xv) "SERPINA1" (SEQ ID No:169) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SERPINA1" encoded by a nucleic acid that hybridizes to the "SERPINA1" nucleic acid or its complement under low stringency conditions,

(xvi) "SIM TO Y71H10A. 2.P" (SEQ ID No:170) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIM TO Y71H10A. 2.P" encoded by a nucleic acid that hybridizes to the "SIM TO Y71H10A. 2.P" nucleic acid or its complement under low stringency conditions,

(xvii) "STX10" (SEQ ID No:150) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX10" encoded by a nucleic acid that hybridizes to the "STX10" nucleic acid or its complement under low stringency conditions,

(xviii) "Sortilin-related receptor" (SEQ ID No:171) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin-related receptor" encoded by a nucleic acid that hybridizes to the "Sortilin-related receptor" nucleic acid or its complement under low stringency conditions,

- (xix) "Thioredoxin domain-containing protein" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,
- (xx) "integral membrane transporter protein" (SEQ ID No:173) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "integral membrane transporter protein" nucleic acid or its complement under low stringency conditions, and/or (xi) "kinectin 1 (kinesin receptor)" (SEQ ID No:174) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "kinectin 1 (kinesin receptor)" encoded by a nucleic acid that hybridizes to the "kinectin 1 (kinesin receptor)" nucleic acid or its complement under low stringency conditions, as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

The invention further relates to the following embodiments of the Bace2-complex

1. A protein complex selected from complex (I) and comprising
 - (a) at least one first protein selected from the group consisting of:
 - (i) "BACE2" (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BACE2" encoded by a nucleic acid that hybridizes to the "BACE2" nucleic acid or its complement under low stringency conditions, and
 - (b) at least one second protein, which second protein is selected from the group consisting of:
 - (i) "APLP2" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,

- (ii) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions,
- (iii) "Calsyntenin 1" (SEQ ID No:158) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin 1" encoded by a nucleic acid that hybridizes to the "Calsyntenin 1" nucleic acid or its complement under low stringency conditions,
- (iv) "Delta-like homolog" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-like homolog" encoded by a nucleic acid that hybridizes to the "Delta-like homolog" nucleic acid or its complement under low stringency conditions,
- (v) "FLJ10474" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ10474" encoded by a nucleic acid that hybridizes to the "FLJ10474" nucleic acid or its complement under low stringency conditions,
- (vi) "FLJ14787" (SEQ ID No:177) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ14787" encoded by a nucleic acid that hybridizes to the "FLJ14787" nucleic acid or its complement under low stringency conditions,
- (vii) "ITCH" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITCH" encoded by a nucleic acid that hybridizes to the "ITCH" nucleic acid or its complement under low stringency conditions,
- (viii) "Integral membrane transporter protein" (SEQ ID No:173) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,
- (ix) "KIAA1949 (FRAGMENT)" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1949 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and

(x) "STX10" (SEQ ID No:150) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX10" encoded by a nucleic acid that hybridizes to the "STX10" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

2. The protein complex according to No. 1 wherein the first protein is the protein Bace2 (SEQ ID NO. 175), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of 'Bace2' encoded by a nucleic acid that hybridizes to the 'Bace2' under low stringency conditions.

3. The protein complex according to No. 1 selected from complex (I) and comprising the following proteins:

- (i) "APLP2" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,
- (ii) "BACE2" (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BACE2" encoded by a nucleic acid that hybridizes to the "BACE2" nucleic acid or its complement under low stringency conditions,
- (iii) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions,
- (iv) "Calsyntenin 1" (SEQ ID No:158) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin 1"

encoded by a nucleic acid that hybridizes to the "Calsyntenin 1" nucleic acid or its complement under low stringency conditions,

(v) "Delta-like homolog" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-like homolog" encoded by a nucleic acid that hybridizes to the "Delta-like homolog" nucleic acid or its complement under low stringency conditions,

(vi) "FLJ10474" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ10474" encoded by a nucleic acid that hybridizes to the "FLJ10474" nucleic acid or its complement under low stringency conditions,

(vii) "FLJ14787" (SEQ ID No:177) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ14787" encoded by a nucleic acid that hybridizes to the "FLJ14787" nucleic acid or its complement under low stringency conditions,

(viii) "ITCH" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITCH" encoded by a nucleic acid that hybridizes to the "ITCH" nucleic acid or its complement under low stringency conditions,

(ix) "Integral membrane transporter protein" (SEQ ID No:173) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,

(x) "KIAA1949 (FRAGMENT)" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1949 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or

(xi) "STX10" (SEQ ID No:150) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX10" encoded by a nucleic acid that hybridizes to the "STX10" nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 9 of the following proteins:

- (i) "APLP2" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,
- (ii) "BACE2" (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BACE2" encoded by a nucleic acid that hybridizes to the "BACE2" nucleic acid or its complement under low stringency conditions,
- (iii) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions,
- (iv) "Calsyntenin 1" (SEQ ID No:158) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin 1" encoded by a nucleic acid that hybridizes to the "Calsyntenin 1" nucleic acid or its complement under low stringency conditions,
- (v) "Delta-like homolog" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-like homolog" encoded by a nucleic acid that hybridizes to the "Delta-like homolog" nucleic acid or its complement under low stringency conditions,
- (vi) "FLJ10474" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ10474" encoded by a nucleic acid that hybridizes to the "FLJ10474" nucleic acid or its complement under low stringency conditions,
- (vii) "FLJ14787" (SEQ ID No:177) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ14787" encoded by a nucleic acid that hybridizes to the "FLJ14787" nucleic acid or its complement under low stringency conditions,
- (viii) "ITCH" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITCH" encoded by a nucleic acid that hybridizes to the "ITCH" nucleic acid or its complement under low stringency conditions,

- (ix) "Integral membrane transporter protein" (SEQ ID No:173) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,
- (x) "KIAA1949 (FRAGMENT)" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1949 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xi) "STX10" (SEQ ID No:150) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX10" encoded by a nucleic acid that hybridizes to the "STX10" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.

6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.

7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.

8. The complex of any of No. 1 - 7 that is involved in the transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP

fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).

9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps: expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.

10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.

11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.

12. Component of the BACE2 obtainable by a process according to any of No. 9 - 11.

13. Protein of the BACE2 selected from

- (i) "FLJ10474" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ10474" encoded by a nucleic acid that hybridizes to the "FLJ10474" nucleic acid or its complement under low stringency conditions,
- (ii) "FLJ14787" (SEQ ID No:177) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ14787" encoded by a nucleic acid that hybridizes to the "FLJ14787" nucleic acid or its complement under low stringency conditions, and
- (iii) "KIAA1949 (FRAGMENT)" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1949

(FRAGMENT)" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

14. Nucleic acid encoding a protein according to No. 13.

15. Construct, preferably a vector construct, comprising (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or

(b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).

16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).

17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and

an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.

18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.

19. The kit according to No. 18 for processing a substrate of said complex.

20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative disease such as Alzheimer's disease;;

21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.

22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.

23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:

(i) "FLJ10474" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ10474" encoded by a nucleic acid that hybridizes to the "FLJ10474" nucleic acid or its complement under low stringency conditions,

(ii) "FLJ14787" (SEQ ID No:177) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ14787" encoded by a nucleic acid that hybridizes to the "FLJ14787" nucleic acid or its complement under low stringency conditions, and/or

(iii) "KIAA1949 (FRAGMENT)" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1949

(FRAGMENT)" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative disease such as Alzheimer's disease;.

25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:

- (i) "FLJ10474" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ10474" encoded by a nucleic acid that hybridizes to the "FLJ10474" nucleic acid or its complement under low stringency conditions,
- (ii) "FLJ14787" (SEQ ID No:177) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ14787" encoded by a nucleic acid that hybridizes to the "FLJ14787" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "KIAA1949 (FRAGMENT)" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1949 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, comprising the steps of
 - (a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and
 - (b) determinig whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of(a) exposing said complex, or a cell or organism containing BACE2 to one or more candidate molecules; and

(b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the

complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.
28. The method of No. 26, wherein the activity of said complex is determined.
29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.
30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.
31. The method of No. 30, wherein said determining step comprises determining whether
 - (i) "APLP2" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions, and/or
 - (ii) "BACE2" (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BACE2" encoded by a nucleic acid that hybridizes to the "BACE2" nucleic acid or its complement under low stringency conditions, and/or
 - (iii) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a

homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions, and/or

(iv) "Calsyntenin 1" (SEQ ID No:158) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin 1" encoded by a nucleic acid that hybridizes to the "Calsyntenin 1" nucleic acid or its complement under low stringency conditions, and/or

(v) "Delta-like homolog" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-like homolog" encoded by a nucleic acid that hybridizes to the "Delta-like homolog" nucleic acid or its complement under low stringency conditions, and/or

(vi) "FLJ10474" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ10474" encoded by a nucleic acid that hybridizes to the "FLJ10474" nucleic acid or its complement under low stringency conditions, and/or

(vii) "FLJ14787" (SEQ ID No:177) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ14787" encoded by a nucleic acid that hybridizes to the "FLJ14787" nucleic acid or its complement under low stringency conditions, and/or

(viii) "ITCH" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITCH" encoded by a nucleic acid that hybridizes to the "ITCH" nucleic acid or its complement under low stringency conditions, and/or

(ix) "Integral membrane transporter protein" (SEQ ID No:173) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions, and/or

(x) "KIAA1949 (FRAGMENT)" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1949 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or

(xi) "STX10" (SEQ ID No:150) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX10" encoded by a

nucleic acid that hybridizes to the "STX10" nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease;.
33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease;.
34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.
35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.
36. The method of No. 35, wherein the amount of said complex is determined.
37. The method of No. 35, wherein the activity of said complex is determined.

38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

40. The method of No. 39, wherein said determining step comprises determining whether
(i) "APLP2" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions, and/or
(ii) "BACE2" (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BACE2" encoded by a nucleic acid that hybridizes to the "BACE2" nucleic acid or its complement under low stringency conditions, and/or
(iii) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions, and/or
(iv) "Calsyntenin 1" (SEQ ID No:158) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin 1" encoded by a nucleic acid that hybridizes to the "Calsyntenin 1" nucleic acid or its complement under low stringency conditions, and/or
(v) "Delta-like homolog" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-like homolog" encoded by a nucleic acid that hybridizes to the "Delta-like homolog" nucleic acid or its complement under low stringency conditions, and/or
(vi) "FLJ10474" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ10474"

encoded by a nucleic acid that hybridizes to the "FLJ10474" nucleic acid or its complement under low stringency conditions, and/or

(vii) "FLJ14787" (SEQ ID No:177) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ14787" encoded by a nucleic acid that hybridizes to the "FLJ14787" nucleic acid or its complement under low stringency conditions, and/or

(viii) "ITCH" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITCH" encoded by a nucleic acid that hybridizes to the "ITCH" nucleic acid or its complement under low stringency conditions, and/or

(ix) "Integral membrane transporter protein" (SEQ ID No:173) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions, and/or

(x) "KIAA1949 (FRAGMENT)" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1949 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or

(xi) "STX10" (SEQ ID No:150) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX10" encoded by a nucleic acid that hybridizes to the "STX10" nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative disease such as Alzheimer's disease;.

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, transactivation of a Gal4-driven reporter gene (e.g. by modifying

the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42 , wherein said disease or disorder involves increased levels of the amount or activity of said complex.

45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins

- (i) "APLP2" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,
- (ii) "BACE2" (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BACE2" encoded by a nucleic acid that hybridizes to the "BACE2" nucleic acid or its complement under low stringency conditions,
- (iii) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions,
- (iv) "Calsyntenin 1" (SEQ ID No:158) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin 1"

encoded by a nucleic acid that hybridizes to the "Calsyntenin 1" nucleic acid or its complement under low stringency conditions,

(v) "Delta-like homolog" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-like homolog" encoded by a nucleic acid that hybridizes to the "Delta-like homolog" nucleic acid or its complement under low stringency conditions,

(vi) "FLJ10474" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ10474" encoded by a nucleic acid that hybridizes to the "FLJ10474" nucleic acid or its complement under low stringency conditions,

(vii) "FLJ14787" (SEQ ID No:177) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ14787" encoded by a nucleic acid that hybridizes to the "FLJ14787" nucleic acid or its complement under low stringency conditions,

(viii) "ITCH" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITCH" encoded by a nucleic acid that hybridizes to the "ITCH" nucleic acid or its complement under low stringency conditions,

(ix) "Integral membrane transporter protein" (SEQ ID No:173) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,

(x) "KIAA1949 (FRAGMENT)" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1949 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or

(xi) "STX10" (SEQ ID No:150) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX10" encoded by a nucleic acid that hybridizes to the "STX10" nucleic acid or its complement under low stringency conditions, as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease;.

The invention further relates to the following embodiments of the Paladin-complex

1. A protein complex selected from complex (I) and comprising
 - (a) at least one first protein selected from the group consisting of:
 - (i) "Paladin" (SEQ ID No:179) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Paladin" encoded by a nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions, and
 - (b) at least one second protein, which second protein is selected from the group consisting of:
 - (i) "AOP2" (SEQ ID No:178) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "AOP2" encoded by a nucleic acid that hybridizes to the "AOP2" nucleic acid or its complement under low stringency conditions,
 - (ii) "Similar to BCL2-associated athanogene 2 (Hypothetical protein)" (SEQ ID No:180) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to BCL2-associated athanogene 2 (Hypothetical protein)" encoded by a nucleic acid that hybridizes to the "Similar to BCL2-associated athanogene 2 (Hypothetical protein)" nucleic acid or its complement under low stringency conditions,
 - (iii) "TNRC6" (SEQ ID No:181) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TNRC6" encoded by a nucleic acid that hybridizes to the "TNRC6" nucleic acid or its complement under low stringency conditions,
 - (iv) "USP7" (SEQ ID No:182) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "USP7" encoded by a nucleic acid that hybridizes to the "USP7" nucleic acid or its complement under low stringency conditions, and
 - (v) "flj11198, member of the abc transporter family" (SEQ ID No:183) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "flj11198, member of the abc transporter family" encoded by a nucleic acid that hybridizes to the "flj11198, member of the abc transporter family" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two

of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

2. The protein complex according to No. 1 wherein the first protein is the protein Paladin (SEQ ID NO. 179), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of 'Paladin' encoded by a nucleic acid that hybridizes to the 'Paladin' under low stringency conditions.
3. The protein complex according to No. 1 selected from complex (I) and comprising the following proteins:
 - (i) "AOP2" (SEQ ID No:178) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "AOP2" encoded by a nucleic acid that hybridizes to the "AOP2" nucleic acid or its complement under low stringency conditions,
 - (ii) "Paladin" (SEQ ID No:179) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Paladin" encoded by a nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions,
 - (iii) "Similar to BCL2-associated athanogene 2 (Hypothetical protein)" (SEQ ID No:180) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to BCL2-associated athanogene 2 (Hypothetical protein)" encoded by a nucleic acid that hybridizes to the "Similar to BCL2-associated athanogene 2 (Hypothetical protein)" nucleic acid or its complement under low stringency conditions,
 - (iv) "TNRC6" (SEQ ID No:181) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TNRC6" encoded by a nucleic acid that hybridizes to the "TNRC6" nucleic acid or its complement under low stringency conditions,

(v) "USP7" (SEQ ID No:182) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "USP7" encoded by a nucleic acid that hybridizes to the "USP7" nucleic acid or its complement under low stringency conditions, and/or

(vi) "flj11198, member of the abc transporter family" (SEQ ID No:183) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "flj11198, member of the abc transporter family" encoded by a nucleic acid that hybridizes to the "flj11198, member of the abc transporter family" nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 4 of the following proteins:

(i) "AOP2" (SEQ ID No:178) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "AOP2" encoded by a nucleic acid that hybridizes to the "AOP2" nucleic acid or its complement under low stringency conditions,

(ii) "Paladin" (SEQ ID No:179) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Paladin" encoded by a nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions,

(iii) "Similar to BCL2-associated athanogene 2 (Hypothetical protein)" (SEQ ID No:180) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to BCL2-associated athanogene 2 (Hypothetical protein)" encoded by a nucleic acid that hybridizes to the "Similar to BCL2-associated athanogene 2 (Hypothetical protein)" nucleic acid or its complement under low stringency conditions,

(iv) "TNRC6" (SEQ ID No:181) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TNRC6" encoded by a nucleic acid that hybridizes to the "TNRC6" nucleic acid or its complement under low stringency conditions,

(v) "USP7" (SEQ ID No:182) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "USP7" encoded by a nucleic acid that hybridizes to the "USP7" nucleic acid or its complement under low stringency conditions,

(vi) "flj11198, member of the abc transporter family" (SEQ ID No:183) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "flj11198, member of the abc transporter family" encoded by a nucleic acid that hybridizes to the "flj11198, member of the abc transporter family" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.
6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.
7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.
8. The complex of any of No. 1 - 7 that is involved in the transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).

9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps: expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.

10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.

11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.

12. Component of the Paladin complex obtainable by a process according to any of No. 9 - 11.

13. Protein of the Paladin complex selected from

(i) "Similar to BCL2-associated athanogene 2 (Hypothetical protein)" (SEQ ID No:180) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to BCL2-associated athanogene 2 (Hypothetical protein)" encoded by a nucleic acid that hybridizes to the "Similar to BCL2-associated athanogene 2 (Hypothetical protein)" nucleic acid or its complement under low stringency conditions,

(ii) "TNRC6" (SEQ ID No:181) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TNRC6" encoded by a nucleic acid that hybridizes to the "TNRC6" nucleic acid or its complement under low stringency conditions, and

(iii) "flj11198, member of the abc transporter family" (SEQ ID No:183) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "flj11198, member of the abc transporter family" encoded by a nucleic acid that hybridizes to the "flj11198, member of the abc transporter family" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured

salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

14. Nucleic acid encoding a protein according to No. 13.
15. Construct, preferably a vector construct, comprising (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or
(b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).
16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).
17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.

18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.

19. The kit according to No. 18 for processing a substrate of said complex.

20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; .

21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.

22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.

23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:

(i) "Similar to BCL2-associated athanogene 2 (Hypothetical protein)" (SEQ ID No:180) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to BCL2-associated athanogene 2 (Hypothetical protein)" encoded by a nucleic acid that hybridizes to the "Similar to BCL2-associated athanogene 2 (Hypothetical protein)" nucleic acid or its complement under low stringency conditions,

(ii) "TNRC6" (SEQ ID No:181) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TNRC6" encoded by a nucleic acid that hybridizes to the "TNRC6" nucleic acid or its complement under low stringency conditions, and/or

(iii) "flj11198, member of the abc transporter family" (SEQ ID No:183) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "flj11198, member of the abc transporter family" encoded by a nucleic acid

that hybridizes to the "flj11198, member of the abc transporter family" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative disease such as Alzheimer's disease; .

25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:

- (i) "Similar to BCL2-associated athanogene 2 (Hypothetical protein)" (SEQ ID No:180) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to BCL2-associated athanogene 2 (Hypothetical protein)" encoded by a nucleic acid that hybridizes to the "Similar to BCL2-associated athanogene 2 (Hypothetical protein)" nucleic acid or its complement under low stringency conditions,
- (ii) "TNRC6" (SEQ ID No:181) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TNRC6" encoded by a nucleic acid that hybridizes to the "TNRC6" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "flj11198, member of the abc transporter family" (SEQ ID No:183) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "flj11198, member of the abc transporter family" encoded by a nucleic acid that hybridizes to the "flj11198, member of the abc transporter family" nucleic acid or its complement under low stringency conditions, comprising the steps of
 - (a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and
 - (b) determinig whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of(a) exposing said complex, or a cell or organism containing Paladin complex to one or more candidate molecules; and

(b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.

28. The method of No. 26, wherein the activity of said complex is determined.

29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.

30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.

31. The method of No. 30, wherein said determining step comprises determining whether

(i) "AOP2" (SEQ ID No:178) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "AOP2" encoded by a nucleic acid that hybridizes to the "AOP2" nucleic acid or its complement under low stringency conditions, and/or

(ii) "Paladin" (SEQ ID No:179) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Paladin" encoded by a nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions, and/or

- (iii) "Similar to BCL2-associated athanogene 2 (Hypothetical protein)" (SEQ ID No:180) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to BCL2-associated athanogene 2 (Hypothetical protein)" encoded by a nucleic acid that hybridizes to the "Similar to BCL2-associated athanogene 2 (Hypothetical protein)" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "TNRC6" (SEQ ID No:181) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TNRC6" encoded by a nucleic acid that hybridizes to the "TNRC6" nucleic acid or its complement under low stringency conditions, and/or
- (v) "USP7" (SEQ ID No:182) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "USP7" encoded by a nucleic acid that hybridizes to the "USP7" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "flj11198, member of the abc transporter family" (SEQ ID No:183) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "flj11198, member of the abc transporter family" encoded by a nucleic acid that hybridizes to the "flj11198, member of the abc transporter family" nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; .

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; .

34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.

37. The method of No. 35, wherein the activity of said complex is determined.

38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

40. The method of No. 39, wherein said determining step comprises determining whether
(i) "AOP2" (SEQ ID No:178) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "AOP2" encoded by a nucleic acid that hybridizes to the "AOP2" nucleic acid or its complement under low stringency conditions, and/or
(ii) "Paladin" (SEQ ID No:179) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Paladin" encoded by a

nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions, and/or

(iii) "Similar to BCL2-associated athanogene 2 (Hypothetical protein)" (SEQ ID No:180) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to BCL2-associated athanogene 2 (Hypothetical protein)" encoded by a nucleic acid that hybridizes to the "Similar to BCL2-associated athanogene 2 (Hypothetical protein)" nucleic acid or its complement under low stringency conditions, and/or

(iv) "TNRC6" (SEQ ID No:181) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TNRC6" encoded by a nucleic acid that hybridizes to the "TNRC6" nucleic acid or its complement under low stringency conditions, and/or

(v) "USP7" (SEQ ID No:182) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "USP7" encoded by a nucleic acid that hybridizes to the "USP7" nucleic acid or its complement under low stringency conditions, and/or

(vi) "flj11198, member of the abc transporter family" (SEQ ID No:183) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "flj11198, member of the abc transporter family" encoded by a nucleic acid that hybridizes to the "flj11198, member of the abc transporter family" nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; .

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of Abeta-40 and

Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42 , wherein said disease or disorder involves increased levels of the amount or activity of said complex.

45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins

(i) "AOP2" (SEQ ID No:178) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "AOP2" encoded by a nucleic acid that hybridizes to the "AOP2" nucleic acid or its complement under low stringency conditions,

(ii) "Paladin" (SEQ ID No:179) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Paladin" encoded by a nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions,

(iii) "Similar to BCL2-associated athanogene 2 (Hypothetical protein)" (SEQ ID No:180) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to BCL2-associated athanogene 2 (Hypothetical protein)" encoded by a nucleic acid that hybridizes to the "Similar to BCL2-associated athanogene 2 (Hypothetical protein)" nucleic acid or its complement under low stringency conditions,

(iv) "TNRC6" (SEQ ID No:181) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TNRC6" encoded by a

nucleic acid that hybridizes to the "TNRC6" nucleic acid or its complement under low stringency conditions,

(v) "USP7" (SEQ ID No:182) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "USP7" encoded by a nucleic acid that hybridizes to the "USP7" nucleic acid or its complement under low stringency conditions, and/or(vi) "flj11198, member of the abc transporter family" (SEQ ID No:183) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "flj11198, member of the abc transporter family" encoded by a nucleic acid that hybridizes to the "flj11198, member of the abc transporter family" nucleic acid or its complement under low stringency conditions,as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; .

The invention further relates to the following embodiments of the TFCP2-complex

1. A protein complex selected from complex (I) and comprising

(a) at least one first protein selected from the group consisting of:

(i) "Fe65" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions, and

(ii) "TFCP2" (SEQ ID No:187) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TFCP2" encoded by a nucleic acid that hybridizes to the "TFCP2" nucleic acid or its complement under low stringency conditions, and

(b) at least one second protein, which second protein is selected from the group consisting of:

(i) "LBP-9" (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LBP-9" encoded by a nucleic acid that hybridizes to the "LBP-9" nucleic acid or its complement under low stringency conditions,

(ii) "RR42_HUMAN" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RR42_HUMAN" encoded by a nucleic acid that hybridizes to the "RR42_HUMAN" nucleic acid or its complement under low stringency conditions,

(iii) "TF LBP-1b" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TF LBP-1b" encoded by a nucleic acid that hybridizes to the "TF LBP-1b" nucleic acid or its complement under low stringency conditions, and

(iv) "TRAP25" (SEQ ID No:188) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TRAP25" encoded by a nucleic acid that hybridizes to the "TRAP25" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

2. The protein complex according to No. 1 wherein the first protein is the protein TFCP2 (SEQ ID NO. 187), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of 'TFCP2' encoded by a nucleic acid that hybridizes to the 'TFCP2' under low stringency conditions.

3. The protein complex according to No. 1 selected from complex (I) and comprising the following proteins:

- (i) "Fe65" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
- (ii) "LBP-9" (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LBP-9" encoded by a

nucleic acid that hybridizes to the "LBP-9" nucleic acid or its complement under low stringency conditions,

(iii) "RR42_HUMAN" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RR42_HUMAN" encoded by a nucleic acid that hybridizes to the "RR42_HUMAN" nucleic acid or its complement under low stringency conditions,

(iv) "TF LBP-1b" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TF LBP-1b" encoded by a nucleic acid that hybridizes to the "TF LBP-1b" nucleic acid or its complement under low stringency conditions,

(v) "TFCP2" (SEQ ID No:187) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TFCP2" encoded by a nucleic acid that hybridizes to the "TFCP2" nucleic acid or its complement under low stringency conditions, and/or

(vi) "TRAP25" (SEQ ID No:188) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TRAP25" encoded by a nucleic acid that hybridizes to the "TRAP25" nucleic acid or its complement under low stringency conditions,

and a protein complex selected from complex (II) and comprising the following proteins:

(i) "LBP-9" (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LBP-9" encoded by a nucleic acid that hybridizes to the "LBP-9" nucleic acid or its complement under low stringency conditions,

(ii) "RR42_HUMAN" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RR42_HUMAN" encoded by a nucleic acid that hybridizes to the "RR42_HUMAN" nucleic acid or its complement under low stringency conditions,

(iii) "TF LBP-1b" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TF LBP-1b" encoded by a nucleic acid that hybridizes to the "TF LBP-1b" nucleic acid or its complement under low stringency conditions,

(iv) "TFCP2" (SEQ ID No:187) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TFCP2" encoded by a

nucleic acid that hybridizes to the "TFCP2" nucleic acid or its complement under low stringency conditions, and/or

(v) "TRAP25" (SEQ ID No:188) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TRAP25" encoded by a nucleic acid that hybridizes to the "TRAP25" nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 3 of the following proteins:

(i) "Fe65" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,

(ii) "LBP-9" (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LBP-9" encoded by a nucleic acid that hybridizes to the "LBP-9" nucleic acid or its complement under low stringency conditions,

(iii) "RR42_HUMAN" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RR42_HUMAN" encoded by a nucleic acid that hybridizes to the "RR42_HUMAN" nucleic acid or its complement under low stringency conditions,

(iv) "TF LBP-1b" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TF LBP-1b" encoded by a nucleic acid that hybridizes to the "TF LBP-1b" nucleic acid or its complement under low stringency conditions,

(v) "TFCP2" (SEQ ID No:187) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TFCP2" encoded by a nucleic acid that hybridizes to the "TFCP2" nucleic acid or its complement under low stringency conditions,

(vi) "TRAP25" (SEQ ID No:188) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TRAP25" encoded by a nucleic acid that hybridizes to the "TRAP25" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.
6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.
7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.
8. The complex of any of No. 1 - 7 that is involved in the transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).
9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps: expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.
10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.
11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.
12. Component of the TFCP2 obtainable by a process according to any of No. 9 - 11.

13. Construct, preferably a vector construct, comprising at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative therof at least one of said proteins, or functionally active fragments or functionally active derivative therof being selected from the first group of proteins according to No. 1(a) and at least one of said proteins, or functionally active fragments of functionally active derivative thereof being selected from the second group of proteins according to No. 1(b).

14. Host cell containing a construct of No. 13 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).

15. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. .

16. A kit comprising in one or more container the complex of any of No. 1 - 8 optionally together with an antibody according to No. 15 and/or further components such as reagents and working instructions.

17. The kit according to No. 16 for processing a substrate of said complex.

18. The kit according to No. 16 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative disease such as Alzheimer's disease;.

19. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one antibody according to No. 15 is attached to a solid carrier.

20. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.
21. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8..
22. A pharmaceutical composition according to No. 21 for the treatment of diseases and disorders such as neurodegenerative disease such as Alzheimer's disease;.
23. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8. comprising the steps of
 - (a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and
 - (b) determinig whether said candidate molecule is bound to the complex or protein.
24. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of
 - (a) exposing said complex, or a cell or organism containing TFCP2 to one or more candidate molecules; and
 - (b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.
25. The method of No. 24, wherein the amount of said complex is determined.

26. The method of No. 24, wherein the activity of said complex is determined.

27. The method of No. 26, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.

28. The method of No. 24, wherein the amount of the individual protein components of said complex are determined.

29. The method of No. 28, wherein said determining step comprises determining whether

(i) "Fe65" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions, and/or

(ii) "LBP-9" (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LBP-9" encoded by a nucleic acid that hybridizes to the "LBP-9" nucleic acid or its complement under low stringency conditions, and/or

(iii) "RR42_HUMAN" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RR42_HUMAN" encoded by a nucleic acid that hybridizes to the "RR42_HUMAN" nucleic acid or its complement under low stringency conditions, and/or

(iv) "TF LBP-1b" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TF LBP-1b" encoded by a nucleic acid that hybridizes to the "TF LBP-1b" nucleic acid or its complement under low stringency conditions, and/or

(v) "TFCP2" (SEQ ID No:187) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TFCP2" encoded by a nucleic acid that hybridizes to the "TFCP2" nucleic acid or its complement under low stringency conditions, and/or

(vi) "TRAP25" (SEQ ID No:188) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TRAP25"

encoded by a nucleic acid that hybridizes to the "TRAP25" nucleic acid or its complement under low stringency conditions, is present in the complex.

30. The method of any of No. 24 - 29, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease;.

31. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease;.

32. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

33. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

34. The method of No. 33, wherein the amount of said complex is determined.

35. The method of No. 33, wherein the activity of said complex is determined.

36. The method of No. 35, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

37. The method of No. 33, wherein the amount of the individual protein components of said complex is determined.

38. The method of No. 37, wherein said determining step comprises determining whether

- (i) "Fe65" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions, and/or
- (ii) "LBP-9" (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LBP-9" encoded by a nucleic acid that hybridizes to the "LBP-9" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "RR42_HUMAN" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RR42_HUMAN" encoded by a nucleic acid that hybridizes to the "RR42_HUMAN" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "TF LBP-1b" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TF LBP-1b" encoded by a nucleic acid that hybridizes to the "TF LBP-1b" nucleic acid or its complement under low stringency conditions, and/or
- (v) "TFCP2" (SEQ ID No:187) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TFCP2" encoded by a nucleic acid that hybridizes to the "TFCP2" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "TRAP25" (SEQ ID No:188) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TRAP25"

encoded by a nucleic acid that hybridizes to the "TRAP25" nucleic acid or its complement under low stringency conditions, is present in the complex.

39. The complex of any one of No. 1 - 8 or the antibody or fragment of No. 15, for use in a method of diagnosing a disease or disorder such as neurodegenerative disease such as Alzheimer's disease;.

40. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

41. The method according to No. 40, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

42. The method according to No. 40 , wherein said disease or disorder involves increased levels of the amount or activity of said complex.

43. Complex of any of No. 1 - 8 and/or protein selected from the following proteins

(i) "Fe65" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,

(ii) "LBP-9" (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LBP-9" encoded by a nucleic acid that hybridizes to the "LBP-9" nucleic acid or its complement under low stringency conditions,

(iii) "RR42_HUMAN" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"RR42_HUMAN" encoded by a nucleic acid that hybridizes to the "RR42_HUMAN" nucleic acid or its complement under low stringency conditions,

(iv) "TF LBP-1b" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TF LBP-1b" encoded by a nucleic acid that hybridizes to the "TF LBP-1b" nucleic acid or its complement under low stringency conditions,

(v) "TFCP2" (SEQ ID No:187) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TFCP2" encoded by a nucleic acid that hybridizes to the "TFCP2" nucleic acid or its complement under low stringency conditions, and/or(vi) "TRAP25" (SEQ ID No:188) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TRAP25" encoded by a nucleic acid that hybridizes to the "TRAP25" nucleic acid or its complement under low stringency conditions,as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease;.

The invention further relates to the following embodiments of the p75 NTR-complex

1. A protein complex selected from complex (I) and comprising
 - (a) at least one first protein selected from the group consisting of:
 - (i) "NRAGE/MAGED1" (SEQ ID No:189) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NRAGE/MAGED1" encoded by a nucleic acid that hybridizes to the "NRAGE/MAGED1" nucleic acid or its complement under low stringency conditions,
 - (ii) "Nogo receptor" (SEQ ID No:190) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nogo receptor" encoded by a nucleic acid that hybridizes to the "Nogo receptor" nucleic acid or its complement under low stringency conditions,
 - (iii) "Rho-GDI" (SEQ ID No:191) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Rho-GDI" encoded by a nucleic acid that hybridizes to the "Rho-GDI" nucleic acid or its complement under low stringency conditions, and

- (iv) "p75 NTR" (SEQ ID No:193) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "p75 NTR" encoded by a nucleic acid that hybridizes to the "p75 NTR" nucleic acid or its complement under low stringency conditions, and
- (b) at least one second protein, which second protein is selected from the group consisting of:
- (i) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions,
 - (ii) "DKFZP586F1524 protein" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DKFZP586F1524 protein" encoded by a nucleic acid that hybridizes to the "DKFZP586F1524 protein" nucleic acid or its complement under low stringency conditions,
 - (iii) "HYPOTHETICAL PROTEIN FLJ39249" (SEQ ID No:162) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ39249" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ39249" nucleic acid or its complement under low stringency conditions,
 - (iv) "Thioredoxin domain-containing protein" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions, and
 - (v) "VAPA" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VAPA" encoded by a nucleic acid that hybridizes to the "VAPA" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl

(pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

2. The protein complex according to No. 1 wherein the first protein is the protein p75 NTR (SEQ ID NO. 193), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of 'p75 NTR' encoded by a nucleic acid that hybridizes to the 'p75 NTR' under low stringency conditions.

3. The protein complex according to No. 1 selected from complex (I) and comprising the following proteins:

- (i) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions,
- (ii) "DKFZP586F1524 protein" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DKFZP586F1524 protein" encoded by a nucleic acid that hybridizes to the "DKFZP586F1524 protein" nucleic acid or its complement under low stringency conditions,
- (iii) "HYPOTHETICAL PROTEIN FLJ39249" (SEQ ID No:162) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ39249" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ39249" nucleic acid or its complement under low stringency conditions,
- (iv) "NRAGE/MAGED1" (SEQ ID No:189) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NRAGE/MAGED1" encoded by a nucleic acid that hybridizes to the "NRAGE/MAGED1" nucleic acid or its complement under low stringency conditions,
- (v) "Nogo receptor" (SEQ ID No:190) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nogo receptor" encoded by a nucleic acid that hybridizes to the "Nogo receptor" nucleic acid or its complement under low stringency conditions,

- (vi) "Rho-GDI" (SEQ ID No:191) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Rho-GDI" encoded by a nucleic acid that hybridizes to the "Rho-GDI" nucleic acid or its complement under low stringency conditions,
- (vii) "Thioredoxin domain-containing protein" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,
- (viii) "VAPA" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VAPA" encoded by a nucleic acid that hybridizes to the "VAPA" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "p75 NTR" (SEQ ID No:193) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "p75 NTR" encoded by a nucleic acid that hybridizes to the "p75 NTR" nucleic acid or its complement under low stringency conditions,
- and a protein complex selected from complex (II) and comprising the following proteins:
- (i) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions,
- (ii) "DKFZP586F1524 protein" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DKFZP586F1524 protein" encoded by a nucleic acid that hybridizes to the "DKFZP586F1524 protein" nucleic acid or its complement under low stringency conditions,
- (iii) "HYPOTHETICAL PROTEIN FLJ39249" (SEQ ID No:162) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ39249" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ39249" nucleic acid or its complement under low stringency conditions,

- (iv) "Thioredoxin domain-containing protein" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,
- (v) "VAPA" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VAPA" encoded by a nucleic acid that hybridizes to the "VAPA" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "p75 NTR" (SEQ ID No:193) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "p75 NTR" encoded by a nucleic acid that hybridizes to the "p75 NTR" nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 4 of the following proteins:

- (i) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions,
- (ii) "DKFZP586F1524 protein" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DKFZP586F1524 protein" encoded by a nucleic acid that hybridizes to the "DKFZP586F1524 protein" nucleic acid or its complement under low stringency conditions,
- (iii) "HYPOTHETICAL PROTEIN FLJ39249" (SEQ ID No:162) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ39249" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ39249" nucleic acid or its complement under low stringency conditions,
- (iv) "NRAGE/MAGED1" (SEQ ID No:189) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"NRAGE/MAGED1" encoded by a nucleic acid that hybridizes to the "NRAGE/MAGED1" nucleic acid or its complement under low stringency conditions,

(v) "Nogo receptor" (SEQ ID No:190) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nogo receptor" encoded by a nucleic acid that hybridizes to the "Nogo receptor" nucleic acid or its complement under low stringency conditions,

(vi) "Rho-GDI" (SEQ ID No:191) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Rho-GDI" encoded by a nucleic acid that hybridizes to the "Rho-GDI" nucleic acid or its complement under low stringency conditions,

(vii) "Thioredoxin domain-containing protein" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,

(viii) "VAPA" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VAPA" encoded by a nucleic acid that hybridizes to the "VAPA" nucleic acid or its complement under low stringency conditions,

(ix) "p75 NTR" (SEQ ID No:193) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "p75 NTR" encoded by a nucleic acid that hybridizes to the "p75 NTR" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.

6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.

7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.
8. The complex of any of No. 1 - 7 that is involved in the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).
9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps: expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.
10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.
11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.
12. Component of the p75 NTR complex obtainable by a process according to any of No. 9 - 11.
13. Protein of the p75 NTR complex selected from

- (i) "DKFZP586F1524 protein" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DKFZP586F1524 protein" encoded by a nucleic acid that hybridizes to the "DKFZP586F1524 protein" nucleic acid or its complement under low stringency conditions, and
- (ii) "HYPOTHETICAL PROTEIN FLJ39249" (SEQ ID No:162) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ39249" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ39249" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

14. Nucleic acid encoding a protein according to No. 13.
15. Construct, preferably a vector construct, comprising (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or
(b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).
16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of

proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).

17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.

18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.

19. The kit according to No. 18 for processing a substrate of said complex.

20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative disease such as Alzheimer's disease;

21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.

22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.

23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:

(i) "DKFZP586F1524 protein" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DKFZP586F1524 protein" encoded by a nucleic acid that hybridizes to the

"DKFZP586F1524 protein" nucleic acid or its complement under low stringency conditions, and/or

(ii) "HYPOTHETICAL PROTEIN FLJ39249" (SEQ ID No:162) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ39249" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ39249" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative disease such as Alzheimer's disease;.

25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:

(i) "DKFZP586F1524 protein" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DKFZP586F1524 protein" encoded by a nucleic acid that hybridizes to the "DKFZP586F1524 protein" nucleic acid or its complement under low stringency conditions, and/or

(ii) "HYPOTHETICAL PROTEIN FLJ39249" (SEQ ID No:162) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ39249" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ39249" nucleic acid or its complement under low stringency conditions, comprising the steps of

(a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and

(b) determinig whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of(a) exposing said complex, or a cell or organism containing p75 NTR complex to one or more candidate molecules; and

(b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.

28. The method of No. 26, wherein the activity of said complex is determined.

29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.

30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.

31. The method of No. 30, wherein said determining step comprises determining whether
(i) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions, and/or
(ii) "DKFZP586F1524 protein" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DKFZP586F1524 protein" encoded by a nucleic acid that hybridizes to the

"DKFZP586F1524 protein" nucleic acid or its complement under low stringency conditions, and/or

(iii) "HYPOTHETICAL PROTEIN FLJ39249" (SEQ ID No:162) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ39249" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ39249" nucleic acid or its complement under low stringency conditions, and/or

(iv) "NRAGE/MAGED1" (SEQ ID No:189) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NRAGE/MAGED1" encoded by a nucleic acid that hybridizes to the "NRAGE/MAGED1" nucleic acid or its complement under low stringency conditions, and/or

(v) "Nogo receptor" (SEQ ID No:190) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nogo receptor" encoded by a nucleic acid that hybridizes to the "Nogo receptor" nucleic acid or its complement under low stringency conditions, and/or

(vi) "Rho-GDI" (SEQ ID No:191) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Rho-GDI" encoded by a nucleic acid that hybridizes to the "Rho-GDI" nucleic acid or its complement under low stringency conditions, and/or

(vii) "Thioredoxin domain-containing protein" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions, and/or

(viii) "VAPA" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VAPA" encoded by a nucleic acid that hybridizes to the "VAPA" nucleic acid or its complement under low stringency conditions, and/or

(ix) "p75 NTR" (SEQ ID No:193) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "p75 NTR" encoded by a nucleic acid that hybridizes to the "p75 NTR" nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease;.

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease;.

34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.

37. The method of No. 35, wherein the activity of said complex is determined.

38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said

complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

40. The method of No. 39, wherein said determining step comprises determining whether

- (i) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions, and/or
- (ii) "DKFZP586F1524 protein" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DKFZP586F1524 protein" encoded by a nucleic acid that hybridizes to the "DKFZP586F1524 protein" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "HYPOTHETICAL PROTEIN FLJ39249" (SEQ ID No:162) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ39249" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ39249" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "NRAGE/MAGED1" (SEQ ID No:189) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NRAGE/MAGED1" encoded by a nucleic acid that hybridizes to the "NRAGE/MAGED1" nucleic acid or its complement under low stringency conditions, and/or
- (v) "Nogo receptor" (SEQ ID No:190) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nogo receptor" encoded by a nucleic acid that hybridizes to the "Nogo receptor" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "Rho-GDI" (SEQ ID No:191) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Rho-GDI"

encoded by a nucleic acid that hybridizes to the "Rho-GDI" nucleic acid or its complement under low stringency conditions, and/or

(vii) "Thioredoxin domain-containing protein" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions, and/or

(viii) "VAPA" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VAPA" encoded by a nucleic acid that hybridizes to the "VAPA" nucleic acid or its complement under low stringency conditions, and/or

(ix) "p75 NTR" (SEQ ID No:193) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "p75 NTR" encoded by a nucleic acid that hybridizes to the "p75 NTR" nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative disease such as Alzheimer's disease;

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a

Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42 , wherein said disease or disorder involves increased levels of the amount or activity of said complex.

45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins

- (i) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions,
- (ii) "DKFZP586F1524 protein" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DKFZP586F1524 protein" encoded by a nucleic acid that hybridizes to the "DKFZP586F1524 protein" nucleic acid or its complement under low stringency conditions,
- (iii) "HYPOTHETICAL PROTEIN FLJ39249" (SEQ ID No:162) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ39249" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ39249" nucleic acid or its complement under low stringency conditions,
- (iv) "NRAGE/MAGED1" (SEQ ID No:189) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NRAGE/MAGED1" encoded by a nucleic acid that hybridizes to the "NRAGE/MAGED1" nucleic acid or its complement under low stringency conditions,
- (v) "Nogo receptor" (SEQ ID No:190) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nogo receptor" encoded by a nucleic acid that hybridizes to the "Nogo receptor" nucleic acid or its complement under low stringency conditions,

- (vi) "Rho-GDI" (SEQ ID No:191) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Rho-GDI" encoded by a nucleic acid that hybridizes to the "Rho-GDI" nucleic acid or its complement under low stringency conditions,
- (vii) "Thioredoxin domain-containing protein" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,
- (viii) "VAPA" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VAPA" encoded by a nucleic acid that hybridizes to the "VAPA" nucleic acid or its complement under low stringency conditions, and/or
 - (ix) "p75 NTR" (SEQ ID No:193) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "p75 NTR" encoded by a nucleic acid that hybridizes to the "p75 NTR" nucleic acid or its complement under low stringency conditions, as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease;.

The invention further relates to the following embodiments of the Lamezin-complex

1. A protein complex selected from complex (I) and comprising
 - (a) at least one first protein selected from the group consisting of:
 - (i) "Lamezin/FKRP" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Lamezin/FKRP" encoded by a nucleic acid that hybridizes to the "Lamezin/FKRP" nucleic acid or its complement under low stringency conditions, and
 - (ii) "Presenilin1 " (SEQ ID No:123) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin1 " encoded by a nucleic acid that hybridizes to the "Presenilin1 " nucleic acid or its complement under low stringency conditions, and
 - (b) at least one second protein, which second protein is selected from the group consisting of:

- (i) "ASPH" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ASPH" encoded by a nucleic acid that hybridizes to the "ASPH" nucleic acid or its complement under low stringency conditions,
- (ii) "C7orf14" (SEQ ID No:195) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C7orf14" encoded by a nucleic acid that hybridizes to the "C7orf14" nucleic acid or its complement under low stringency conditions,
- (iii) "CLNS1A" (SEQ ID No:196) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CLNS1A" encoded by a nucleic acid that hybridizes to the "CLNS1A" nucleic acid or its complement under low stringency conditions,
- (iv) "CLU: clusterin (complement lysis inhibitor, SP-40,40, sulfated glycoprotein 2, testosterone-repressed prostate message 2, apolipoprotein J)" (SEQ ID No:197) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CLU: clusterin (complement lysis inhibitor, SP-40,40, sulfated glycoprotein 2, testosterone-repressed prostate message 2, apolipoprotein J)" encoded by a nucleic acid that hybridizes to the "CLU: clusterin (complement lysis inhibitor, SP-40,40, sulfated glycoprotein 2, testosterone-repressed prostate message 2, apolipoprotein J)" nucleic acid or its complement under low stringency conditions,
- (v) "CNTNAP1" (SEQ ID No:198) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CNTNAP1" encoded by a nucleic acid that hybridizes to the "CNTNAP1" nucleic acid or its complement under low stringency conditions,
- (vi) "COX5B" (SEQ ID No:199) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COX5B" encoded by a nucleic acid that hybridizes to the "COX5B" nucleic acid or its complement under low stringency conditions,
- (vii) "COX6B" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COX6B" encoded by a nucleic acid that hybridizes to the "COX6B" nucleic acid or its complement under low stringency conditions,
- (viii) "COX6C" (SEQ ID No:201) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COX6C"

encoded by a nucleic acid that hybridizes to the "COX6C" nucleic acid or its complement under low stringency conditions,

(ix) "CSGlcA-T" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CSGlcA-T" encoded by a nucleic acid that hybridizes to the "CSGlcA-T" nucleic acid or its complement under low stringency conditions,

(x) "DICER1" (SEQ ID No:202) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DICER1" encoded by a nucleic acid that hybridizes to the "DICER1" nucleic acid or its complement under low stringency conditions,

(xi) "DREV1" (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DREV1" encoded by a nucleic acid that hybridizes to the "DREV1" nucleic acid or its complement under low stringency conditions,

(xii) "EC 6.3.2.19 (Fragment)" (SEQ ID No:204) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EC 6.3.2.19 (Fragment)" encoded by a nucleic acid that hybridizes to the "EC 6.3.2.19 (Fragment)" nucleic acid or its complement under low stringency conditions,

(xiii) "EIF2B2" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EIF2B2" encoded by a nucleic acid that hybridizes to the "EIF2B2" nucleic acid or its complement under low stringency conditions,

(xiv) "EXTL2" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXTL2" encoded by a nucleic acid that hybridizes to the "EXTL2" nucleic acid or its complement under low stringency conditions,

(xv) "G2AN" (SEQ ID No:207) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "G2AN" encoded by a nucleic acid that hybridizes to the "G2AN" nucleic acid or its complement under low stringency conditions,

(xvi) "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" (SEQ ID No:208) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" encoded by a nucleic acid that hybridizes to the

- "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" nucleic acid or its complement under low stringency conditions,
- (xvii) "HIV-1 Vpr-binding protein (Fragment)" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HIV-1 Vpr-binding protein (Fragment)" encoded by a nucleic acid that hybridizes to the "HIV-1 Vpr-binding protein (Fragment)" nucleic acid or its complement under low stringency conditions,
- (xviii) "HPIP" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HPIP" encoded by a nucleic acid that hybridizes to the "HPIP" nucleic acid or its complement under low stringency conditions,
- (xix) "HSPC329 (Fragment)" (SEQ ID No:211) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC329 (Fragment)" encoded by a nucleic acid that hybridizes to the "HSPC329 (Fragment)" nucleic acid or its complement under low stringency conditions,
- (xx) "HYPOTHETICAL PROTEIN" (SEQ ID No:212) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN" nucleic acid or its complement under low stringency conditions,
- (xxi) "HYPOTHETICAL PROTEIN" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN" nucleic acid or its complement under low stringency conditions,
- (xxii) "HYPOTHETICAL PROTEIN KIAA1524 (FRAGMENT)" (SEQ ID No:214) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN KIAA1524 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN KIAA1524 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xxiii) "Hypothetical protein FLJ34763" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ34763" encoded by a nucleic acid that hybridizes to

the "Hypothetical protein FLJ34763" nucleic acid or its complement under low stringency conditions,

(xxiv) "Hypothetical protein KIAA0062 (Fragment)" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0062 (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0062 (Fragment)" nucleic acid or its complement under low stringency conditions,

(xxv) "Hypothetical protein KIAA1500 (Fragment)" (SEQ ID No:217) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA1500 (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA1500 (Fragment)" nucleic acid or its complement under low stringency conditions,

(xxvi) "IGF2R" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IGF2R" encoded by a nucleic acid that hybridizes to the "IGF2R" nucleic acid or its complement under low stringency conditions,

(xxvii) "ITGAV" (SEQ ID No:219) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITGAV" encoded by a nucleic acid that hybridizes to the "ITGAV" nucleic acid or its complement under low stringency conditions,

(xxviii) "ITPR2" (SEQ ID No:220) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITPR2" encoded by a nucleic acid that hybridizes to the "ITPR2" nucleic acid or its complement under low stringency conditions,

(xxix) "KIAA1250, homolog of rat kinase D-interacting substance of 220 kDa" (SEQ ID No:164) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250, homolog of rat kinase D-interacting substance of 220 kDa" encoded by a nucleic acid that hybridizes to the "KIAA1250, homolog of rat kinase D-interacting substance of 220 kDa" nucleic acid or its complement under low stringency conditions,

(xxx) "LPHH1" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LPHH1" encoded by a nucleic acid that hybridizes to the "LPHH1" nucleic acid or its complement under low stringency conditions,

- (xxxi) "Laminin, gamma 1 " (SEQ ID No:88) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Laminin, gamma 1 " encoded by a nucleic acid that hybridizes to the "Laminin, gamma 1 " nucleic acid or its complement under low stringency conditions,
- (xxxii) "MAGEB4" (SEQ ID No:223) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MAGEB4" encoded by a nucleic acid that hybridizes to the "MAGEB4" nucleic acid or its complement under low stringency conditions,
- (xxxiii) "MGC5442" (SEQ ID No:224) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,
- (xxxiv) "Neural cell adhesion molecule L1 " (SEQ ID No:225) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neural cell adhesion molecule L1 " encoded by a nucleic acid that hybridizes to the "Neural cell adhesion molecule L1 " nucleic acid or its complement under low stringency conditions,
- (xxxv) "Neurotrypsin" (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,
- (xxxvi) "Nuclear protein SDK3" (SEQ ID No:226) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nuclear protein SDK3" encoded by a nucleic acid that hybridizes to the "Nuclear protein SDK3" nucleic acid or its complement under low stringency conditions,
- (xxxvii) "PPIB" (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPIB" encoded by a nucleic acid that hybridizes to the "PPIB" nucleic acid or its complement under low stringency conditions,
- (xxxviii) "PTDSS1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PTDSS1" encoded by a nucleic acid that hybridizes to the "PTDSS1" nucleic acid or its complement under low stringency conditions,

- (xxxix) "Reelin" (SEQ ID No:97) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Reelin" encoded by a nucleic acid that hybridizes to the "Reelin" nucleic acid or its complement under low stringency conditions,
- (xli) "SCG2" (SEQ ID No:229) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SCG2" encoded by a nucleic acid that hybridizes to the "SCG2" nucleic acid or its complement under low stringency conditions,
- (xlii) "SIMILAR TO HYPOTHETICAL PROTEIN SB153" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO HYPOTHETICAL PROTEIN SB153" encoded by a nucleic acid that hybridizes to the "SIMILAR TO HYPOTHETICAL PROTEIN SB153" nucleic acid or its complement under low stringency conditions,
- (xliii) "STRA6 isoform 1" (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STRA6 isoform 1" encoded by a nucleic acid that hybridizes to the "STRA6 isoform 1" nucleic acid or its complement under low stringency conditions,
- (xlvi) "Similar to RIKEN cDNA 1100001L14 gene (Fragment)" (SEQ ID No:232) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to RIKEN cDNA 1100001L14 gene (Fragment)" encoded by a nucleic acid that hybridizes to the "Similar to RIKEN cDNA 1100001L14 gene (Fragment)" nucleic acid or its complement under low stringency conditions,
- (xlv) "TLOC1" (SEQ ID No:233) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TLOC1" encoded by a nucleic acid that hybridizes to the "TLOC1" nucleic acid or its complement under low stringency conditions,
- (xlvi) "VESICULAR INTEGRAL-MEMBRANE PROTEIN VIP36 PRECURSOR" (SEQ ID No:234) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VESICULAR INTEGRAL-MEMBRANE PROTEIN VIP36 PRECURSOR" encoded by a nucleic acid that hybridizes to the "VESICULAR INTEGRAL-MEMBRANE PROTEIN VIP36 PRECURSOR" nucleic acid or its complement under low stringency conditions,
- (xlvii) "Wolframin" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Wolframin"

encoded by a nucleic acid that hybridizes to the "Wolframin" nucleic acid or its complement under low stringency conditions,

(xlvii) "bzw1: basic leucine zipper and w2 domains 1" (SEQ ID No:236) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "bzw1: basic leucine zipper and w2 domains 1" encoded by a nucleic acid that hybridizes to the "bzw1: basic leucine zipper and w2 domains 1" nucleic acid or its complement under low stringency conditions,

(xlviii) "dkfzp586c1924" (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "dkfzp586c1924" encoded by a nucleic acid that hybridizes to the "dkfzp586c1924" nucleic acid or its complement under low stringency conditions,

(xl ix) "ensp00000258417" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ensp00000258417" encoded by a nucleic acid that hybridizes to the "ensp00000258417" nucleic acid or its complement under low stringency conditions, and

(I) "hyou1: hypoxia up-regulated 1" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hyou1: hypoxia up-regulated 1" encoded by a nucleic acid that hybridizes to the "hyou1: hypoxia up-regulated 1" nucleic acid or its complement under low stringency conditions,

(II) "UGCGL2" (SEQ ID No:102) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "UGCGL2" encoded by a nucleic acid that hybridizes to the "UGCGL2" nucleic acid or its complement under low stringency conditions,

and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

2. The protein complex according to No. 1 wherein the first protein is the protein Lamezin (SEQ ID NO. 222), or a functionally active derivative thereof, or a functionally active

fragment thereof, or a homolog thereof, or a variant of 'Lamezin' encoded by a nucleic acid that hybridizes to the 'Lamezin' under low stringency conditions.

3. The protein complex according to No. 1 selected from complex (I) and comprising the following proteins:

- (i) "ASPH" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ASPH" encoded by a nucleic acid that hybridizes to the "ASPH" nucleic acid or its complement under low stringency conditions,
- (ii) "C7orf14" (SEQ ID No:195) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C7orf14" encoded by a nucleic acid that hybridizes to the "C7orf14" nucleic acid or its complement under low stringency conditions,
- (iii) "CLNS1A" (SEQ ID No:196) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CLNS1A" encoded by a nucleic acid that hybridizes to the "CLNS1A" nucleic acid or its complement under low stringency conditions,
- (iv) "CLU: clusterin (complement lysis inhibitor, SP-40,40, sulfated glycoprotein 2, testosterone-repressed prostate message 2, apolipoprotein J)" (SEQ ID No:197) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CLU: clusterin (complement lysis inhibitor, SP-40,40, sulfated glycoprotein 2, testosterone-repressed prostate message 2, apolipoprotein J)" encoded by a nucleic acid that hybridizes to the "CLU: clusterin (complement lysis inhibitor, SP-40,40, sulfated glycoprotein 2, testosterone-repressed prostate message 2, apolipoprotein J)" nucleic acid or its complement under low stringency conditions,
- (v) "CNTNAP1" (SEQ ID No:198) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CNTNAP1" encoded by a nucleic acid that hybridizes to the "CNTNAP1" nucleic acid or its complement under low stringency conditions,
- (vi) "COX5B" (SEQ ID No:199) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COX5B" encoded by a nucleic acid that hybridizes to the "COX5B" nucleic acid or its complement under low stringency conditions,

- (vii) "COX6B" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COX6B" encoded by a nucleic acid that hybridizes to the "COX6B" nucleic acid or its complement under low stringency conditions,
- (viii) "COX6C" (SEQ ID No:201) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COX6C" encoded by a nucleic acid that hybridizes to the "COX6C" nucleic acid or its complement under low stringency conditions,
- (ix) "CSGlcA-T" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CSGlcA-T" encoded by a nucleic acid that hybridizes to the "CSGlcA-T" nucleic acid or its complement under low stringency conditions,
- (x) "DICER1" (SEQ ID No:202) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DICER1" encoded by a nucleic acid that hybridizes to the "DICER1" nucleic acid or its complement under low stringency conditions,
- (xi) "DREV1" (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DREV1" encoded by a nucleic acid that hybridizes to the "DREV1" nucleic acid or its complement under low stringency conditions,
- (xii) "EC 6.3.2.19 (Fragment)" (SEQ ID No:204) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EC 6.3.2.19 (Fragment)" encoded by a nucleic acid that hybridizes to the "EC 6.3.2.19 (Fragment)" nucleic acid or its complement under low stringency conditions,
- (xiii) "EIF2B2" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EIF2B2" encoded by a nucleic acid that hybridizes to the "EIF2B2" nucleic acid or its complement under low stringency conditions,
- (xiv) "EXTL2" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXTL2" encoded by a nucleic acid that hybridizes to the "EXTL2" nucleic acid or its complement under low stringency conditions,
- (xv) "G2AN" (SEQ ID No:207) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "G2AN" encoded by a

nucleic acid that hybridizes to the "G2AN" nucleic acid or its complement under low stringency conditions,

(xvi) "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" (SEQ ID No:208) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" encoded by a nucleic acid that hybridizes to the "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" nucleic acid or its complement under low stringency conditions,

(xvii) "HIV-1 Vpr-binding protein (Fragment)" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HIV-1 Vpr-binding protein (Fragment)" encoded by a nucleic acid that hybridizes to the "HIV-1 Vpr-binding protein (Fragment)" nucleic acid or its complement under low stringency conditions,

(xviii) "HPIP" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HPIP" encoded by a nucleic acid that hybridizes to the "HPIP" nucleic acid or its complement under low stringency conditions,

(xix) "HSPC329 (Fragment)" (SEQ ID No:211) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC329 (Fragment)" encoded by a nucleic acid that hybridizes to the "HSPC329 (Fragment)" nucleic acid or its complement under low stringency conditions,

(xx) "HYPOTHETICAL PROTEIN" (SEQ ID No:212) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN" nucleic acid or its complement under low stringency conditions,

(xxi) "HYPOTHETICAL PROTEIN" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN" nucleic acid or its complement under low stringency conditions,

(xxii) "HYPOTHETICAL PROTEIN KIAA1524 (FRAGMENT)" (SEQ ID No:214) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN KIAA1524 (FRAGMENT)"

encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN KIAA1524 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xxiii) "Hypothetical protein FLJ34763" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ34763" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ34763" nucleic acid or its complement under low stringency conditions,

(xxiv) "Hypothetical protein KIAA0062 (Fragment)" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0062 (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0062 (Fragment)" nucleic acid or its complement under low stringency conditions,

(xxv) "Hypothetical protein KIAA1500 (Fragment)" (SEQ ID No:217) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA1500 (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA1500 (Fragment)" nucleic acid or its complement under low stringency conditions,

(xxvi) "IGF2R" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IGF2R" encoded by a nucleic acid that hybridizes to the "IGF2R" nucleic acid or its complement under low stringency conditions,

(xxvii) "ITGAV" (SEQ ID No:219) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITGAV" encoded by a nucleic acid that hybridizes to the "ITGAV" nucleic acid or its complement under low stringency conditions,

(xxviii) "ITPR2" (SEQ ID No:220) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITPR2" encoded by a nucleic acid that hybridizes to the "ITPR2" nucleic acid or its complement under low stringency conditions,

(xxix) "KIAA1250, homolog of rat kinase D-interacting substance of 220 kDa" (SEQ ID No:164) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250, homolog of rat kinase D-interacting substance of 220 kDa" encoded by a nucleic acid that hybridizes to the

"KIAA1250, homolog of rat kinase D-interacting substance of 220 kDa" nucleic acid or its complement under low stringency conditions,

(xxx) "LPHH1" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LPHH1" encoded by a nucleic acid that hybridizes to the "LPHH1" nucleic acid or its complement under low stringency conditions,

(xxxi) "Lamezin/FKRP" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Lamezin/FKRP" encoded by a nucleic acid that hybridizes to the "Lamezin/FKRP" nucleic acid or its complement under low stringency conditions,

(xxxii) "Laminin, gamma 1 " (SEQ ID No:88) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Laminin, gamma 1 " encoded by a nucleic acid that hybridizes to the "Laminin, gamma 1 " nucleic acid or its complement under low stringency conditions,

(xxxiii) "MAGEB4" (SEQ ID No:223) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MAGEB4" encoded by a nucleic acid that hybridizes to the "MAGEB4" nucleic acid or its complement under low stringency conditions,

(xxxiv) "MGC5442" (SEQ ID No:224) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,

(xxxv) "Neural cell adhesion molecule L1 " (SEQ ID No:225) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neural cell adhesion molecule L1 " encoded by a nucleic acid that hybridizes to the "Neural cell adhesion molecule L1 " nucleic acid or its complement under low stringency conditions,

(xxxvi) "Neurotrypsin" (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,

(xxxvii) "Nuclear protein SDK3" (SEQ ID No:226) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"Nuclear protein SDK3" encoded by a nucleic acid that hybridizes to the "Nuclear protein SDK3" nucleic acid or its complement under low stringency conditions,

(xxxviii) "PPIB" (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPIB" encoded by a nucleic acid that hybridizes to the "PPIB" nucleic acid or its complement under low stringency conditions,

(xxxix) "PTDSS1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PTDSS1" encoded by a nucleic acid that hybridizes to the "PTDSS1" nucleic acid or its complement under low stringency conditions,

(xi) "Presenilin1 " (SEQ ID No:123) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin1 " encoded by a nucleic acid that hybridizes to the "Presenilin1 " nucleic acid or its complement under low stringency conditions,

(xli) "Reelin" (SEQ ID No:97) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Reelin" encoded by a nucleic acid that hybridizes to the "Reelin" nucleic acid or its complement under low stringency conditions,

(xlii) "SCG2" (SEQ ID No:229) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SCG2" encoded by a nucleic acid that hybridizes to the "SCG2" nucleic acid or its complement under low stringency conditions,

(xliii) "SIMILAR TO HYPOTHETICAL PROTEIN SB153" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO HYPOTHETICAL PROTEIN SB153" encoded by a nucleic acid that hybridizes to the "SIMILAR TO HYPOTHETICAL PROTEIN SB153" nucleic acid or its complement under low stringency conditions,

(xlv) "STRA6 isoform 1" (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STRA6 isoform 1" encoded by a nucleic acid that hybridizes to the "STRA6 isoform 1" nucleic acid or its complement under low stringency conditions,

(xlv) "Similar to RIKEN cDNA 1100001L14 gene (Fragment)" (SEQ ID No:232) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to RIKEN cDNA 1100001L14 gene (Fragment)"

encoded by a nucleic acid that hybridizes to the "Similar to RIKEN cDNA 1100001L14 gene (Fragment)" nucleic acid or its complement under low stringency conditions,

(xlvi) "TLOC1" (SEQ ID No:233) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TLOC1" encoded by a nucleic acid that hybridizes to the "TLOC1" nucleic acid or its complement under low stringency conditions,

(xlvii) "UGCGL2" (SEQ ID No:102) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "UGCGL2" encoded by a nucleic acid that hybridizes to the "UGCGL2" nucleic acid or its complement under low stringency conditions,

(xlviii) "VESICULAR INTEGRAL-MEMBRANE PROTEIN VIP36 PRECURSOR" (SEQ ID No:234) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VESICULAR INTEGRAL-MEMBRANE PROTEIN VIP36 PRECURSOR" encoded by a nucleic acid that hybridizes to the "VESICULAR INTEGRAL-MEMBRANE PROTEIN VIP36 PRECURSOR" nucleic acid or its complement under low stringency conditions,

(xlix) "Wolframin" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Wolframin" encoded by a nucleic acid that hybridizes to the "Wolframin" nucleic acid or its complement under low stringency conditions,

(I) "bzw1: basic leucine zipper and w2 domains 1" (SEQ ID No:236) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "bzw1: basic leucine zipper and w2 domains 1" encoded by a nucleic acid that hybridizes to the "bzw1: basic leucine zipper and w2 domains 1" nucleic acid or its complement under low stringency conditions,

(ii) "dkfzp586c1924" (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "dkfzp586c1924" encoded by a nucleic acid that hybridizes to the "dkfzp586c1924" nucleic acid or its complement under low stringency conditions,

(iii) "ensp00000258417" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ensp00000258417" encoded by a nucleic acid that hybridizes to the "ensp00000258417" nucleic acid or its complement under low stringency conditions,

and/or

(liii) "hyou1: hypoxia up-regulated 1" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hyou1: hypoxia up-regulated 1" encoded by a nucleic acid that hybridizes to the "hyou1: hypoxia up-regulated 1" nucleic acid or its complement under low stringency conditions, and a protein complex selected from complex (II) and comprising the following proteins:

(i) "ASPH" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ASPH" encoded by a nucleic acid that hybridizes to the "ASPH" nucleic acid or its complement under low stringency conditions,

(ii) "C7orf14" (SEQ ID No:195) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C7orf14" encoded by a nucleic acid that hybridizes to the "C7orf14" nucleic acid or its complement under low stringency conditions,

(iii) "CLNS1A" (SEQ ID No:196) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CLNS1A" encoded by a nucleic acid that hybridizes to the "CLNS1A" nucleic acid or its complement under low stringency conditions,

(iv) "CLU: clusterin (complement lysis inhibitor, SP-40,40, sulfated glycoprotein 2, testosterone-repressed prostate message 2, apolipoprotein J)" (SEQ ID No:197) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CLU: clusterin (complement lysis inhibitor, SP-40,40, sulfated glycoprotein 2, testosterone-repressed prostate message 2, apolipoprotein J)" encoded by a nucleic acid that hybridizes to the "CLU: clusterin (complement lysis inhibitor, SP-40,40, sulfated glycoprotein 2, testosterone-repressed prostate message 2, apolipoprotein J)" nucleic acid or its complement under low stringency conditions,

(v) "CNTNAP1" (SEQ ID No:198) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CNTNAP1" encoded by a nucleic acid that hybridizes to the "CNTNAP1" nucleic acid or its complement under low stringency conditions,

(vi) "COX5B" (SEQ ID No:199) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COX5B" encoded by a nucleic acid that hybridizes to the "COX5B" nucleic acid or its complement under low stringency conditions,

- (vii) "COX6B" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COX6B" encoded by a nucleic acid that hybridizes to the "COX6B" nucleic acid or its complement under low stringency conditions,
- (viii) "COX6C" (SEQ ID No:201) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COX6C" encoded by a nucleic acid that hybridizes to the "COX6C" nucleic acid or its complement under low stringency conditions,
- (ix) "CSGlcA-T" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CSGlcA-T" encoded by a nucleic acid that hybridizes to the "CSGlcA-T" nucleic acid or its complement under low stringency conditions,
- (x) "DICER1" (SEQ ID No:202) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DICER1" encoded by a nucleic acid that hybridizes to the "DICER1" nucleic acid or its complement under low stringency conditions,
- (xi) "DREV1" (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DREV1" encoded by a nucleic acid that hybridizes to the "DREV1" nucleic acid or its complement under low stringency conditions,
- (xii) "EC 6.3.2.19 (Fragment)" (SEQ ID No:204) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EC 6.3.2.19 (Fragment)" encoded by a nucleic acid that hybridizes to the "EC 6.3.2.19 (Fragment)" nucleic acid or its complement under low stringency conditions,
- (xiii) "EIF2B2" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EIF2B2" encoded by a nucleic acid that hybridizes to the "EIF2B2" nucleic acid or its complement under low stringency conditions,
- (xiv) "EXTL2" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXTL2" encoded by a nucleic acid that hybridizes to the "EXTL2" nucleic acid or its complement under low stringency conditions,
- (xv) "G2AN" (SEQ ID No:207) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "G2AN" encoded by a

nucleic acid that hybridizes to the "G2AN" nucleic acid or its complement under low stringency conditions,

(xvi) "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" (SEQ ID No:208) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" encoded by a nucleic acid that hybridizes to the "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" nucleic acid or its complement under low stringency conditions,

(xvii) "HIV-1 Vpr-binding protein (Fragment)" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HIV-1 Vpr-binding protein (Fragment)" encoded by a nucleic acid that hybridizes to the "HIV-1 Vpr-binding protein (Fragment)" nucleic acid or its complement under low stringency conditions,

(xviii) "HPIP" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HPIP" encoded by a nucleic acid that hybridizes to the "HPIP" nucleic acid or its complement under low stringency conditions,

(xix) "HSPC329 (Fragment)" (SEQ ID No:211) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC329 (Fragment)" encoded by a nucleic acid that hybridizes to the "HSPC329 (Fragment)" nucleic acid or its complement under low stringency conditions,

(xx) "HYPOTHETICAL PROTEIN" (SEQ ID No:212) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN" nucleic acid or its complement under low stringency conditions,

(xxi) "HYPOTHETICAL PROTEIN" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN" nucleic acid or its complement under low stringency conditions,

(xxii) "HYPOTHETICAL PROTEIN KIAA1524 (FRAGMENT)" (SEQ ID No:214) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN KIAA1524 (FRAGMENT)"

encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN KIAA1524 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xxiii) "Hypothetical protein FLJ34763" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ34763" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ34763" nucleic acid or its complement under low stringency conditions,

(xxiv) "Hypothetical protein KIAA0062 (Fragment)" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0062 (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0062 (Fragment)" nucleic acid or its complement under low stringency conditions,

(xxv) "Hypothetical protein KIAA1500 (Fragment)" (SEQ ID No:217) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA1500 (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA1500 (Fragment)" nucleic acid or its complement under low stringency conditions,

(xxvi) "IGF2R" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IGF2R" encoded by a nucleic acid that hybridizes to the "IGF2R" nucleic acid or its complement under low stringency conditions,

(xxvii) "ITGAV" (SEQ ID No:219) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITGAV" encoded by a nucleic acid that hybridizes to the "ITGAV" nucleic acid or its complement under low stringency conditions,

(xxviii) "ITPR2" (SEQ ID No:220) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITPR2" encoded by a nucleic acid that hybridizes to the "ITPR2" nucleic acid or its complement under low stringency conditions,

(xxix) "KIAA1250, homolog of rat kinase D-interacting substance of 220 kDa" (SEQ ID No:164) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250, homolog of rat kinase D-interacting substance of 220 kDa" encoded by a nucleic acid that hybridizes to the

- "KIAA1250, homolog of rat kinase D-interacting substance of 220 kDa" nucleic acid or its complement under low stringency conditions,
- (xxx) "LPHH1" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LPHH1" encoded by a nucleic acid that hybridizes to the "LPHH1" nucleic acid or its complement under low stringency conditions,
- (xxxi) "Lamezin/FKRP" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Lamezin/FKRP" encoded by a nucleic acid that hybridizes to the "Lamezin/FKRP" nucleic acid or its complement under low stringency conditions,
- (xxxii) "Laminin, gamma 1 " (SEQ ID No:88) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Laminin, gamma 1 " encoded by a nucleic acid that hybridizes to the "Laminin, gamma 1 " nucleic acid or its complement under low stringency conditions,
- (xxxiii) "MAGEB4" (SEQ ID No:223) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MAGEB4" encoded by a nucleic acid that hybridizes to the "MAGEB4" nucleic acid or its complement under low stringency conditions,
- (xxxiv) "MGC5442" (SEQ ID No:224) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,
- (xxxv) "Neural cell adhesion molecule L1 " (SEQ ID No:225) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neural cell adhesion molecule L1 " encoded by a nucleic acid that hybridizes to the "Neural cell adhesion molecule L1 " nucleic acid or its complement under low stringency conditions,
- (xxxvi) "Neurotrypsin" (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,
- (xxxvii) "Nuclear protein SDK3" (SEQ ID No:226) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"Nuclear protein SDK3" encoded by a nucleic acid that hybridizes to the "Nuclear protein SDK3" nucleic acid or its complement under low stringency conditions,

(xxxviii) "PPIB" (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPIB" encoded by a nucleic acid that hybridizes to the "PPIB" nucleic acid or its complement under low stringency conditions,

(xxxix) "PTDSS1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PTDSS1" encoded by a nucleic acid that hybridizes to the "PTDSS1" nucleic acid or its complement under low stringency conditions,

(xli) "Reelin" (SEQ ID No:97) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Reelin" encoded by a nucleic acid that hybridizes to the "Reelin" nucleic acid or its complement under low stringency conditions,

(xli) "SCG2" (SEQ ID No:229) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SCG2" encoded by a nucleic acid that hybridizes to the "SCG2" nucleic acid or its complement under low stringency conditions,

(xlii) "SIMILAR TO HYPOTHETICAL PROTEIN SB153" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO HYPOTHETICAL PROTEIN SB153" encoded by a nucleic acid that hybridizes to the "SIMILAR TO HYPOTHETICAL PROTEIN SB153" nucleic acid or its complement under low stringency conditions,

(xliii) "STRA6 isoform 1" (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STRA6 isoform 1" encoded by a nucleic acid that hybridizes to the "STRA6 isoform 1" nucleic acid or its complement under low stringency conditions,

(xliv) "Similar to RIKEN cDNA 1100001L14 gene (Fragment)" (SEQ ID No:232) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to RIKEN cDNA 1100001L14 gene (Fragment)" encoded by a nucleic acid that hybridizes to the "Similar to RIKEN cDNA 1100001L14 gene (Fragment)" nucleic acid or its complement under low stringency conditions,

(xlv) "TLOC1" (SEQ ID No:233) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TLOC1"

encoded by a nucleic acid that hybridizes to the "TLOC1" nucleic acid or its complement under low stringency conditions,

(xlvi) "VESICULAR INTEGRAL-MEMBRANE PROTEIN VIP36 PRECURSOR" (SEQ ID No:234) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VESICULAR INTEGRAL-MEMBRANE PROTEIN VIP36 PRECURSOR" encoded by a nucleic acid that hybridizes to the "VESICULAR INTEGRAL-MEMBRANE PROTEIN VIP36 PRECURSOR" nucleic acid or its complement under low stringency conditions,

(xlvii) "Wolframin" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Wolframin" encoded by a nucleic acid that hybridizes to the "Wolframin" nucleic acid or its complement under low stringency conditions,

(xviii) "bzw1: basic leucine zipper and w2 domains 1" (SEQ ID No:236) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "bzw1: basic leucine zipper and w2 domains 1" encoded by a nucleic acid that hybridizes to the "bzw1: basic leucine zipper and w2 domains 1" nucleic acid or its complement under low stringency conditions,

(xlix) "dkfzp586c1924" (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "dkfzp586c1924" encoded by a nucleic acid that hybridizes to the "dkfzp586c1924" nucleic acid or its complement under low stringency conditions,

(I) "ensp00000258417" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ensp00000258417" encoded by a nucleic acid that hybridizes to the "ensp00000258417" nucleic acid or its complement under low stringency conditions, and/or

(ii) "hyou1: hypoxia up-regulated 1" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hyou1: hypoxia up-regulated 1" encoded by a nucleic acid that hybridizes to the "hyou1: hypoxia up-regulated 1" nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 49 of the following proteins:

- (i) "ASPH" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ASPH" encoded by a nucleic acid that hybridizes to the "ASPH" nucleic acid or its complement under low stringency conditions,
- (ii) "C7orf14" (SEQ ID No:195) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C7orf14" encoded by a nucleic acid that hybridizes to the "C7orf14" nucleic acid or its complement under low stringency conditions,
- (iii) "CLNS1A" (SEQ ID No:196) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CLNS1A" encoded by a nucleic acid that hybridizes to the "CLNS1A" nucleic acid or its complement under low stringency conditions,
- (iv) "CLU: clusterin (complement lysis inhibitor, SP-40,40, sulfated glycoprotein 2, testosterone-repressed prostate message 2, apolipoprotein J)" (SEQ ID No:197) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CLU: clusterin (complement lysis inhibitor, SP-40,40, sulfated glycoprotein 2, testosterone-repressed prostate message 2, apolipoprotein J)" encoded by a nucleic acid that hybridizes to the "CLU: clusterin (complement lysis inhibitor, SP-40,40, sulfated glycoprotein 2, testosterone-repressed prostate message 2, apolipoprotein J)" nucleic acid or its complement under low stringency conditions,
- (v) "CNTNAP1" (SEQ ID No:198) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CNTNAP1" encoded by a nucleic acid that hybridizes to the "CNTNAP1" nucleic acid or its complement under low stringency conditions,
- (vi) "COX5B" (SEQ ID No:199) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COX5B" encoded by a nucleic acid that hybridizes to the "COX5B" nucleic acid or its complement under low stringency conditions,
- (vii) "COX6B" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COX6B" encoded by a nucleic acid that hybridizes to the "COX6B" nucleic acid or its complement under low stringency conditions,
- (viii) "COX6C" (SEQ ID No:201) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COX6C"

encoded by a nucleic acid that hybridizes to the "COX6C" nucleic acid or its complement under low stringency conditions,

(ix) "CSGlcA-T" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CSGlcA-T" encoded by a nucleic acid that hybridizes to the "CSGlcA-T" nucleic acid or its complement under low stringency conditions,

(x) "DICER1" (SEQ ID No:202) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DICER1" encoded by a nucleic acid that hybridizes to the "DICER1" nucleic acid or its complement under low stringency conditions,

(xi) "DREV1" (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DREV1" encoded by a nucleic acid that hybridizes to the "DREV1" nucleic acid or its complement under low stringency conditions,

(xii) "EC 6.3.2.19 (Fragment)" (SEQ ID No:204) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EC 6.3.2.19 (Fragment)" encoded by a nucleic acid that hybridizes to the "EC 6.3.2.19 (Fragment)" nucleic acid or its complement under low stringency conditions,

(xiii) "EIF2B2" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EIF2B2" encoded by a nucleic acid that hybridizes to the "EIF2B2" nucleic acid or its complement under low stringency conditions,

(xiv) "EXTL2" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXTL2" encoded by a nucleic acid that hybridizes to the "EXTL2" nucleic acid or its complement under low stringency conditions,

(xv) "G2AN" (SEQ ID No:207) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "G2AN" encoded by a nucleic acid that hybridizes to the "G2AN" nucleic acid or its complement under low stringency conditions,

(xvi) "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" (SEQ ID No:208) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" encoded by a nucleic acid that hybridizes to the

"Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" nucleic acid or its complement under low stringency conditions,

(xvii) "HIV-1 Vpr-binding protein (Fragment)" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HIV-1 Vpr-binding protein (Fragment)" encoded by a nucleic acid that hybridizes to the "HIV-1 Vpr-binding protein (Fragment)" nucleic acid or its complement under low stringency conditions,

(xviii) "HPIP" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HPIP" encoded by a nucleic acid that hybridizes to the "HPIP" nucleic acid or its complement under low stringency conditions,

(xix) "HSPC329 (Fragment)" (SEQ ID No:211) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC329 (Fragment)" encoded by a nucleic acid that hybridizes to the "HSPC329 (Fragment)" nucleic acid or its complement under low stringency conditions,

(xx) "HYPOTHETICAL PROTEIN" (SEQ ID No:212) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN" nucleic acid or its complement under low stringency conditions,

(xxi) "HYPOTHETICAL PROTEIN" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN" nucleic acid or its complement under low stringency conditions,

(xxii) "HYPOTHETICAL PROTEIN KIAA1524 (FRAGMENT)" (SEQ ID No:214) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN KIAA1524 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN KIAA1524 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xxiii) "Hypothetical protein FLJ34763" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ34763" encoded by a nucleic acid that hybridizes to

the "Hypothetical protein FLJ34763" nucleic acid or its complement under low stringency conditions,

(xxiv) "Hypothetical protein KIAA0062 (Fragment)" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0062 (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0062 (Fragment)" nucleic acid or its complement under low stringency conditions,

(xxv) "Hypothetical protein KIAA1500 (Fragment)" (SEQ ID No:217) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA1500 (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA1500 (Fragment)" nucleic acid or its complement under low stringency conditions,

(xxvi) "IGF2R" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IGF2R" encoded by a nucleic acid that hybridizes to the "IGF2R" nucleic acid or its complement under low stringency conditions,

(xxvii) "ITGAV" (SEQ ID No:219) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITGAV" encoded by a nucleic acid that hybridizes to the "ITGAV" nucleic acid or its complement under low stringency conditions,

(xxviii) "ITPR2" (SEQ ID No:220) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITPR2" encoded by a nucleic acid that hybridizes to the "ITPR2" nucleic acid or its complement under low stringency conditions,

(xxix) "KIAA1250, homolog of rat kinase D-interacting substance of 220 kDa" (SEQ ID No:164) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250, homolog of rat kinase D-interacting substance of 220 kDa" encoded by a nucleic acid that hybridizes to the "KIAA1250, homolog of rat kinase D-interacting substance of 220 kDa" nucleic acid or its complement under low stringency conditions,

(xxx) "LPHH1" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LPHH1" encoded by a nucleic acid that hybridizes to the "LPHH1" nucleic acid or its complement under low stringency conditions,

- (xxxii) "Lamezin/FKRP" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Lamezin/FKRP" encoded by a nucleic acid that hybridizes to the "Lamezin/FKRP" nucleic acid or its complement under low stringency conditions,
- (xxxiii) "Laminin, gamma 1 " (SEQ ID No:88) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Laminin, gamma 1 " encoded by a nucleic acid that hybridizes to the "Laminin, gamma 1 " nucleic acid or its complement under low stringency conditions,
- (xxxiv) "MAGEB4" (SEQ ID No:223) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MAGEB4" encoded by a nucleic acid that hybridizes to the "MAGEB4" nucleic acid or its complement under low stringency conditions,
- (xxxv) "Neural cell adhesion molecule L1 " (SEQ ID No:225) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neural cell adhesion molecule L1 " encoded by a nucleic acid that hybridizes to the "Neural cell adhesion molecule L1 " nucleic acid or its complement under low stringency conditions,
- (xxxvi) "Neurotrypsin" (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,
- (xxxvii) "Nuclear protein SDK3" (SEQ ID No:226) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nuclear protein SDK3" encoded by a nucleic acid that hybridizes to the "Nuclear protein SDK3" nucleic acid or its complement under low stringency conditions,
- (xxxviii) "PPIB" (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPIB" encoded by a nucleic acid that hybridizes to the "PPIB" nucleic acid or its complement under low stringency conditions,

- (xxxix) "PTDSS1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PTDSS1" encoded by a nucleic acid that hybridizes to the "PTDSS1" nucleic acid or its complement under low stringency conditions,
- (xli) "Presenilin1 " (SEQ ID No:123) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin1 " encoded by a nucleic acid that hybridizes to the "Presenilin1 " nucleic acid or its complement under low stringency conditions,
- (xli) "Reelin" (SEQ ID No:97) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Reelin" encoded by a nucleic acid that hybridizes to the "Reelin" nucleic acid or its complement under low stringency conditions,
- (xlii) "SCG2" (SEQ ID No:229) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SCG2" encoded by a nucleic acid that hybridizes to the "SCG2" nucleic acid or its complement under low stringency conditions,
- (xliii) "SIMILAR TO HYPOTHETICAL PROTEIN SB153" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO HYPOTHETICAL PROTEIN SB153" encoded by a nucleic acid that hybridizes to the "SIMILAR TO HYPOTHETICAL PROTEIN SB153" nucleic acid or its complement under low stringency conditions,
- (xliv) "STRA6 isoform 1" (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STRA6 isoform 1" encoded by a nucleic acid that hybridizes to the "STRA6 isoform 1" nucleic acid or its complement under low stringency conditions,
- (xlv) "Similar to RIKEN cDNA 1100001L14 gene (Fragment)" (SEQ ID No:232) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to RIKEN cDNA 1100001L14 gene (Fragment)" encoded by a nucleic acid that hybridizes to the "Similar to RIKEN cDNA 1100001L14 gene (Fragment)" nucleic acid or its complement under low stringency conditions,
- (xlvi) "TLOC1" (SEQ ID No:233) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TLOC1" encoded by a nucleic acid that hybridizes to the "TLOC1" nucleic acid or its complement under low stringency conditions,

- (xlvi) "UGCGL2" (SEQ ID No:102) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "UGCGL2" encoded by a nucleic acid that hybridizes to the "UGCGL2" nucleic acid or its complement under low stringency conditions,
- (xlviii) "VESICULAR INTEGRAL-MEMBRANE PROTEIN VIP36 PRECURSOR" (SEQ ID No:234) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VESICULAR INTEGRAL-MEMBRANE PROTEIN VIP36 PRECURSOR" encoded by a nucleic acid that hybridizes to the "VESICULAR INTEGRAL-MEMBRANE PROTEIN VIP36 PRECURSOR" nucleic acid or its complement under low stringency conditions,
- (xlxi) "Wolframin" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Wolframin" encoded by a nucleic acid that hybridizes to the "Wolframin" nucleic acid or its complement under low stringency conditions,
- (I) "bzw1: basic leucine zipper and w2 domains 1" (SEQ ID No:236) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "bzw1: basic leucine zipper and w2 domains 1" encoded by a nucleic acid that hybridizes to the "bzw1: basic leucine zipper and w2 domains 1" nucleic acid or its complement under low stringency conditions,
- (II) "dkfzp586c1924" (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "dkfzp586c1924" encoded by a nucleic acid that hybridizes to the "dkfzp586c1924" nucleic acid or its complement under low stringency conditions,
- (III) "ensp00000258417" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ensp00000258417" encoded by a nucleic acid that hybridizes to the "ensp00000258417" nucleic acid or its complement under low stringency conditions,
- (liii) "hyou1: hypoxia up-regulated 1" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hyou1: hypoxia up-regulated 1" encoded by a nucleic acid that hybridizes to the "hyou1: hypoxia up-regulated 1" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.
6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.
7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.
8. The complex of any of No. 1 - 7 that is involved in the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).
9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps: expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.

10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.

11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.

12. Component of the Lamezin complex obtainable by a process according to any of No. 9 - 11.

13. Protein of the Lamezin complex selected from

(i) "C7orf14" (SEQ ID No:195) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C7orf14" encoded by a nucleic acid that hybridizes to the "C7orf14" nucleic acid or its complement under low stringency conditions,

(ii) "CSGlcA-T" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CSGlcA-T" encoded by a nucleic acid that hybridizes to the "CSGlcA-T" nucleic acid or its complement under low stringency conditions,

(iii) "DREV1" (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DREV1" encoded by a nucleic acid that hybridizes to the "DREV1" nucleic acid or its complement under low stringency conditions,

(iv) "EXTL2" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXTL2" encoded by a nucleic acid that hybridizes to the "EXTL2" nucleic acid or its complement under low stringency conditions,

(v) "HIV-1 Vpr-binding protein (Fragment)" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HIV-1 Vpr-binding protein (Fragment)" encoded by a nucleic acid that hybridizes to the "HIV-1 Vpr-binding protein (Fragment)" nucleic acid or its complement under low stringency conditions,

(vi) "HPIP" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HPIP" encoded by a

nucleic acid that hybridizes to the "HPIP" nucleic acid or its complement under low stringency conditions,

(vii) "HSPC329 (Fragment)" (SEQ ID No:211) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC329 (Fragment)" encoded by a nucleic acid that hybridizes to the "HSPC329 (Fragment)" nucleic acid or its complement under low stringency conditions,

(viii) "HYPOTHETICAL PROTEIN" (SEQ ID No:212) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN" nucleic acid or its complement under low stringency conditions,

(ix) "HYPOTHETICAL PROTEIN" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN" nucleic acid or its complement under low stringency conditions,

(x) "HYPOTHETICAL PROTEIN KIAA1524 (FRAGMENT)" (SEQ ID No:214) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN KIAA1524 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN KIAA1524 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xi) "Hypothetical protein FLJ34763" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ34763" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ34763" nucleic acid or its complement under low stringency conditions,

(xii) "Hypothetical protein KIAA0062 (Fragment)" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0062 (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0062 (Fragment)" nucleic acid or its complement under low stringency conditions,

(xiii) "Hypothetical protein KIAA1500 (Fragment)" (SEQ ID No:217) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA1500 (Fragment)" encoded by a nucleic acid

that hybridizes to the "Hypothetical protein KIAA1500 (Fragment)" nucleic acid or its complement under low stringency conditions,

(xiv) "KIAA1250, homolog of rat kinase D-interacting substance of 220 kDa" (SEQ ID No:164) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250, homolog of rat kinase D-interacting substance of 220 kDa" encoded by a nucleic acid that hybridizes to the "KIAA1250, homolog of rat kinase D-interacting substance of 220 kDa" nucleic acid or its complement under low stringency conditions,

(xv) "MAGEB4" (SEQ ID No:223) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MAGEB4" encoded by a nucleic acid that hybridizes to the "MAGEB4" nucleic acid or its complement under low stringency conditions,

(xvi) "MGC5442" (SEQ ID No:224) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,

(xvii) "SIMILAR TO HYPOTHETICAL PROTEIN SB153" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO HYPOTHETICAL PROTEIN SB153" encoded by a nucleic acid that hybridizes to the "SIMILAR TO HYPOTHETICAL PROTEIN SB153" nucleic acid or its complement under low stringency conditions,

(xviii) "STRA6 isoform 1" (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STRA6 isoform 1" encoded by a nucleic acid that hybridizes to the "STRA6 isoform 1" nucleic acid or its complement under low stringency conditions,

(xix) "Similar to RIKEN cDNA 1100001L14 gene (Fragment)" (SEQ ID No:232) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to RIKEN cDNA 1100001L14 gene (Fragment)" encoded by a nucleic acid that hybridizes to the "Similar to RIKEN cDNA 1100001L14 gene (Fragment)" nucleic acid or its complement under low stringency conditions,

(xx) "VESICULAR INTEGRAL-MEMBRANE PROTEIN VIP36 PRECURSOR" (SEQ ID No:234) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VESICULAR INTEGRAL-MEMBRANE PROTEIN VIP36 PRECURSOR" encoded by a nucleic acid that hybridizes to the

"VESICULAR INTEGRAL-MEMBRANE PROTEIN VIP36 PRECURSOR" nucleic acid or its complement under low stringency conditions,

(xxi) "Wolframin" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Wolframin" encoded by a nucleic acid that hybridizes to the "Wolframin" nucleic acid or its complement under low stringency conditions,

(xxii) "bzw1: basic leucine zipper and w2 domains 1" (SEQ ID No:236) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "bzw1: basic leucine zipper and w2 domains 1" encoded by a nucleic acid that hybridizes to the "bzw1: basic leucine zipper and w2 domains 1" nucleic acid or its complement under low stringency conditions,

(xxiii) "dkfzp586c1924" (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "dkfzp586c1924" encoded by a nucleic acid that hybridizes to the "dkfzp586c1924" nucleic acid or its complement under low stringency conditions,

(xxiv) "ensp00000258417" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ensp00000258417" encoded by a nucleic acid that hybridizes to the "ensp00000258417" nucleic acid or its complement under low stringency conditions, and

(xxv) "hyou1: hypoxia up-regulated 1" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hyou1: hypoxia up-regulated 1" encoded by a nucleic acid that hybridizes to the "hyou1: hypoxia up-regulated 1" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

14. Nucleic acid encoding a protein according to No. 13.

15. Construct, preferably a vector construct, comprising (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or

(b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).

16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).

17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.

18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.

19. The kit according to No. 18 for processing a substrate of said complex.

20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative disease such as

Alzheimer's disease, congenital muscular dystrophy 1C and limb-girdle muscular dystrophy 2;.

21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.

22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.

23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:

- (i) "C7orf14" (SEQ ID No:195) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C7orf14" encoded by a nucleic acid that hybridizes to the "C7orf14" nucleic acid or its complement under low stringency conditions,
- (ii) "CSGlcA-T" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CSGlcA-T" encoded by a nucleic acid that hybridizes to the "CSGlcA-T" nucleic acid or its complement under low stringency conditions,
- (iii) "DREV1" (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DREV1" encoded by a nucleic acid that hybridizes to the "DREV1" nucleic acid or its complement under low stringency conditions,
- (iv) "EXTL2" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXTL2" encoded by a nucleic acid that hybridizes to the "EXTL2" nucleic acid or its complement under low stringency conditions,
- (v) "HIV-1 Vpr-binding protein (Fragment)" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HIV-1 Vpr-binding protein (Fragment)" encoded by a nucleic acid that hybridizes to the "HIV-1 Vpr-binding protein (Fragment)" nucleic acid or its complement under low stringency conditions,

- (vi) "HPIP" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HPIP" encoded by a nucleic acid that hybridizes to the "HPIP" nucleic acid or its complement under low stringency conditions,
- (vii) "HSPC329 (Fragment)" (SEQ ID No:211) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC329 (Fragment)" encoded by a nucleic acid that hybridizes to the "HSPC329 (Fragment)" nucleic acid or its complement under low stringency conditions,
- (viii) "HYPOTHETICAL PROTEIN" (SEQ ID No:212) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN" nucleic acid or its complement under low stringency conditions,
- (ix) "HYPOTHETICAL PROTEIN" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN" nucleic acid or its complement under low stringency conditions,
- (x) "HYPOTHETICAL PROTEIN KIAA1524 (FRAGMENT)" (SEQ ID No:214) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN KIAA1524 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN KIAA1524 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xi) "Hypothetical protein FLJ34763" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ34763" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ34763" nucleic acid or its complement under low stringency conditions,
- (xii) "Hypothetical protein KIAA0062 (Fragment)" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0062 (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0062 (Fragment)" nucleic acid or its complement under low stringency conditions,

- (xiii) "Hypothetical protein KIAA1500 (Fragment)" (SEQ ID No:217) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA1500 (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA1500 (Fragment)" nucleic acid or its complement under low stringency conditions,
- (xiv) "KIAA1250, homolog of rat kinase D-interacting substance of 220 kDa" (SEQ ID No:164) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250, homolog of rat kinase D-interacting substance of 220 kDa" encoded by a nucleic acid that hybridizes to the "KIAA1250, homolog of rat kinase D-interacting substance of 220 kDa" nucleic acid or its complement under low stringency conditions,
- (xv) "MAGEB4" (SEQ ID No:223) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MAGEB4" encoded by a nucleic acid that hybridizes to the "MAGEB4" nucleic acid or its complement under low stringency conditions,
- (xvi) "MGC5442" (SEQ ID No:224) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,
- (xvii) "SIMILAR TO HYPOTHETICAL PROTEIN SB153" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO HYPOTHETICAL PROTEIN SB153" encoded by a nucleic acid that hybridizes to the "SIMILAR TO HYPOTHETICAL PROTEIN SB153" nucleic acid or its complement under low stringency conditions,
- (xviii) "STRA6 isoform 1" (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STRA6 isoform 1" encoded by a nucleic acid that hybridizes to the "STRA6 isoform 1" nucleic acid or its complement under low stringency conditions,
- (xix) "Similar to RIKEN cDNA 1100001L14 gene (Fragment)" (SEQ ID No:232) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to RIKEN cDNA 1100001L14 gene (Fragment)" encoded by a nucleic acid that hybridizes to the "Similar to RIKEN cDNA 1100001L14 gene (Fragment)" nucleic acid or its complement under low stringency conditions,

(xx) "VESICULAR INTEGRAL-MEMBRANE PROTEIN VIP36 PRECURSOR" (SEQ ID No:234) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VESICULAR INTEGRAL-MEMBRANE PROTEIN VIP36 PRECURSOR" encoded by a nucleic acid that hybridizes to the "VESICULAR INTEGRAL-MEMBRANE PROTEIN VIP36 PRECURSOR" nucleic acid or its complement under low stringency conditions,

(xxi) "Wolframin" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Wolframin" encoded by a nucleic acid that hybridizes to the "Wolframin" nucleic acid or its complement under low stringency conditions,

(xxii) "bzw1: basic leucine zipper and w2 domains 1" (SEQ ID No:236) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "bzw1: basic leucine zipper and w2 domains 1" encoded by a nucleic acid that hybridizes to the "bzw1: basic leucine zipper and w2 domains 1" nucleic acid or its complement under low stringency conditions,

(xxiii) "dkfzp586c1924" (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "dkfzp586c1924" encoded by a nucleic acid that hybridizes to the "dkfzp586c1924" nucleic acid or its complement under low stringency conditions,

(xxiv) "ensp00000258417" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ensp00000258417" encoded by a nucleic acid that hybridizes to the "ensp00000258417" nucleic acid or its complement under low stringency conditions,

and/or

(xxv) "hyou1: hypoxia up-regulated 1" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hyou1: hypoxia up-regulated 1" encoded by a nucleic acid that hybridizes to the "hyou1: hypoxia up-regulated 1" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative disease such as Alzheimer's disease, congenital muscular dystrophy 1C and limb-girdle muscular dystrophy 2;

25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:

- (i) "C7orf14" (SEQ ID No:195) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C7orf14" encoded by a nucleic acid that hybridizes to the "C7orf14" nucleic acid or its complement under low stringency conditions,
- (ii) "CSGlcA-T" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CSGlcA-T" encoded by a nucleic acid that hybridizes to the "CSGlcA-T" nucleic acid or its complement under low stringency conditions,
- (iii) "DREV1" (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DREV1" encoded by a nucleic acid that hybridizes to the "DREV1" nucleic acid or its complement under low stringency conditions,
- (iv) "EXTL2" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXTL2" encoded by a nucleic acid that hybridizes to the "EXTL2" nucleic acid or its complement under low stringency conditions,
- (v) "HIV-1 Vpr-binding protein (Fragment)" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HIV-1 Vpr-binding protein (Fragment)" encoded by a nucleic acid that hybridizes to the "HIV-1 Vpr-binding protein (Fragment)" nucleic acid or its complement under low stringency conditions,
- (vi) "HPIP" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HPIP" encoded by a nucleic acid that hybridizes to the "HPIP" nucleic acid or its complement under low stringency conditions,
- (vii) "HSPC329 (Fragment)" (SEQ ID No:211) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC329 (Fragment)" encoded by a nucleic acid that hybridizes to the "HSPC329 (Fragment)" nucleic acid or its complement under low stringency conditions,

- (viii) "HYPOTHETICAL PROTEIN" (SEQ ID No:212) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN" nucleic acid or its complement under low stringency conditions,
- (ix) "HYPOTHETICAL PROTEIN" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN" nucleic acid or its complement under low stringency conditions,
- (x) "HYPOTHETICAL PROTEIN KIAA1524 (FRAGMENT)" (SEQ ID No:214) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN KIAA1524 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN KIAA1524 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xi) "Hypothetical protein FLJ34763" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ34763" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ34763" nucleic acid or its complement under low stringency conditions,
- (xii) "Hypothetical protein KIAA0062 (Fragment)" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0062 (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0062 (Fragment)" nucleic acid or its complement under low stringency conditions,
- (xiii) "Hypothetical protein KIAA1500 (Fragment)" (SEQ ID No:217) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA1500 (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA1500 (Fragment)" nucleic acid or its complement under low stringency conditions,
- (xiv) "KIAA1250, homolog of rat kinase D-interacting substance of 220 kDa" (SEQ ID No:164) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250, homolog of rat kinase D-interacting substance of 220 kDa" encoded by a nucleic acid that hybridizes to the

"KIAA1250, homolog of rat kinase D-interacting substance of 220 kDa" nucleic acid or its complement under low stringency conditions,

(xv) "MAGEB4" (SEQ ID No:223) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MAGEB4" encoded by a nucleic acid that hybridizes to the "MAGEB4" nucleic acid or its complement under low stringency conditions,

(xvi) "MGC5442" (SEQ ID No:224) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,

(xvii) "SIMILAR TO HYPOTHETICAL PROTEIN SB153" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO HYPOTHETICAL PROTEIN SB153" encoded by a nucleic acid that hybridizes to the "SIMILAR TO HYPOTHETICAL PROTEIN SB153" nucleic acid or its complement under low stringency conditions,

(xviii) "STRA6 isoform 1" (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STRA6 isoform 1" encoded by a nucleic acid that hybridizes to the "STRA6 isoform 1" nucleic acid or its complement under low stringency conditions,

(xix) "Similar to RIKEN cDNA 1100001L14 gene (Fragment)" (SEQ ID No:232) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to RIKEN cDNA 1100001L14 gene (Fragment)" encoded by a nucleic acid that hybridizes to the "Similar to RIKEN cDNA 1100001L14 gene (Fragment)" nucleic acid or its complement under low stringency conditions,

(xx) "VESICULAR INTEGRAL-MEMBRANE PROTEIN VIP36 PRECURSOR" (SEQ ID No:234) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VESICULAR INTEGRAL-MEMBRANE PROTEIN VIP36 PRECURSOR" encoded by a nucleic acid that hybridizes to the "VESICULAR INTEGRAL-MEMBRANE PROTEIN VIP36 PRECURSOR" nucleic acid or its complement under low stringency conditions,

(xxi) "Wolframin" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Wolframin" encoded by a nucleic acid that hybridizes to the "Wolframin" nucleic acid or its complement under low stringency conditions,

- (xxii) "bzw1: basic leucine zipper and w2 domains 1" (SEQ ID No:236) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "bzw1: basic leucine zipper and w2 domains 1" encoded by a nucleic acid that hybridizes to the "bzw1: basic leucine zipper and w2 domains 1" nucleic acid or its complement under low stringency conditions,
- (xxiii) "dkfzp586c1924" (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "dkfzp586c1924" encoded by a nucleic acid that hybridizes to the "dkfzp586c1924" nucleic acid or its complement under low stringency conditions,
- (xxiv) "ensp00000258417" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ensp00000258417" encoded by a nucleic acid that hybridizes to the "ensp00000258417" nucleic acid or its complement under low stringency conditions, and/or
- (xxv) "hyou1: hypoxia up-regulated 1" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hyou1: hypoxia up-regulated 1" encoded by a nucleic acid that hybridizes to the "hyou1: hypoxia up-regulated 1" nucleic acid or its complement under low stringency conditions, comprising the steps of
- (a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and
- (b) determining whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of (a) exposing said complex, or a cell or organism containing Lamezin complex to one or more candidate molecules; and

(b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity,

protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.
28. The method of No. 26, wherein the activity of said complex is determined.
29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.
30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.
31. The method of No. 30, wherein said determining step comprises determining whether
 - (i) "ASPH" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ASPH" encoded by a nucleic acid that hybridizes to the "ASPH" nucleic acid or its complement under low stringency conditions, and/or
 - (ii) "C7orf14" (SEQ ID No:195) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C7orf14" encoded by a nucleic acid that hybridizes to the "C7orf14" nucleic acid or its complement under low stringency conditions, and/or
 - (iii) "CLNS1A" (SEQ ID No:196) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CLNS1A" encoded by a nucleic acid that hybridizes to the "CLNS1A" nucleic acid or its complement under low stringency conditions, and/or
 - (iv) "CLU: clusterin (complement lysis inhibitor, SP-40,40, sulfated glycoprotein 2, testosterone-repressed prostate message 2, apolipoprotein J)" (SEQ ID No:197) or a

functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CLU: clusterin (complement lysis inhibitor, SP-40,40, sulfated glycoprotein 2, testosterone-repressed prostate message 2, apolipoprotein J)" encoded by a nucleic acid that hybridizes to the "CLU: clusterin (complement lysis inhibitor, SP-40,40, sulfated glycoprotein 2, testosterone-repressed prostate message 2, apolipoprotein J)" nucleic acid or its complement under low stringency conditions, and/or

(v) "CNTNAP1" (SEQ ID No:198) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CNTNAP1" encoded by a nucleic acid that hybridizes to the "CNTNAP1" nucleic acid or its complement under low stringency conditions, and/or

(vi) "COX5B" (SEQ ID No:199) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COX5B" encoded by a nucleic acid that hybridizes to the "COX5B" nucleic acid or its complement under low stringency conditions, and/or

(vii) "COX6B" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COX6B" encoded by a nucleic acid that hybridizes to the "COX6B" nucleic acid or its complement under low stringency conditions, and/or

(viii) "COX6C" (SEQ ID No:201) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COX6C" encoded by a nucleic acid that hybridizes to the "COX6C" nucleic acid or its complement under low stringency conditions, and/or

(ix) "CSGlcA-T" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CSGlcA-T" encoded by a nucleic acid that hybridizes to the "CSGlcA-T" nucleic acid or its complement under low stringency conditions, and/or

(x) "DICER1" (SEQ ID No:202) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DICER1" encoded by a nucleic acid that hybridizes to the "DICER1" nucleic acid or its complement under low stringency conditions, and/or

(xi) "DREV1" (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DREV1" encoded by a nucleic acid that hybridizes to the "DREV1" nucleic acid or its complement under low stringency conditions, and/or

- (xii) "EC 6.3.2.19 (Fragment)" (SEQ ID No:204) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EC 6.3.2.19 (Fragment)" encoded by a nucleic acid that hybridizes to the "EC 6.3.2.19 (Fragment)" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "EIF2B2" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EIF2B2" encoded by a nucleic acid that hybridizes to the "EIF2B2" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "EXTL2" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXTL2" encoded by a nucleic acid that hybridizes to the "EXTL2" nucleic acid or its complement under low stringency conditions, and/or
- (xv) "G2AN" (SEQ ID No:207) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "G2AN" encoded by a nucleic acid that hybridizes to the "G2AN" nucleic acid or its complement under low stringency conditions, and/or
- (xvi) "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" (SEQ ID No:208) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" encoded by a nucleic acid that hybridizes to the "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" nucleic acid or its complement under low stringency conditions, and/or
- (xvii) "HIV-1 Vpr-binding protein (Fragment)" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HIV-1 Vpr-binding protein (Fragment)" encoded by a nucleic acid that hybridizes to the "HIV-1 Vpr-binding protein (Fragment)" nucleic acid or its complement under low stringency conditions, and/or
- (xviii) "HPIP" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HPIP" encoded by a nucleic acid that hybridizes to the "HPIP" nucleic acid or its complement under low stringency conditions, and/or
- (xix) "HSPC329 (Fragment)" (SEQ ID No:211) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC329

- (Fragment)" encoded by a nucleic acid that hybridizes to the "HSPC329 (Fragment)" nucleic acid or its complement under low stringency conditions, and/or
- (xx) "HYPOTHETICAL PROTEIN" (SEQ ID No:212) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN" nucleic acid or its complement under low stringency conditions, and/or
- (xxi) "HYPOTHETICAL PROTEIN" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN" nucleic acid or its complement under low stringency conditions, and/or
- (xxii) "HYPOTHETICAL PROTEIN KIAA1524 (FRAGMENT)" (SEQ ID No:214) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN KIAA1524 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN KIAA1524 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or
- (xxiii) "Hypothetical protein FLJ34763" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ34763" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ34763" nucleic acid or its complement under low stringency conditions, and/or
- (xxiv) "Hypothetical protein KIAA0062 (Fragment)" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0062 (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0062 (Fragment)" nucleic acid or its complement under low stringency conditions, and/or
- (xxv) "Hypothetical protein KIAA1500 (Fragment)" (SEQ ID No:217) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA1500 (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA1500 (Fragment)" nucleic acid or its complement under low stringency conditions, and/or
- (xxvi) "IGF2R" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IGF2R"

encoded by a nucleic acid that hybridizes to the "IGF2R" nucleic acid or its complement under low stringency conditions, and/or

(xxvii) "ITGAV" (SEQ ID No:219) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITGAV" encoded by a nucleic acid that hybridizes to the "ITGAV" nucleic acid or its complement under low stringency conditions, and/or

(xxviii) "ITPR2" (SEQ ID No:220) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITPR2" encoded by a nucleic acid that hybridizes to the "ITPR2" nucleic acid or its complement under low stringency conditions, and/or

(xxix) "KIAA1250, homolog of rat kinase D-interacting substance of 220 kDa" (SEQ ID No:164) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250, homolog of rat kinase D-interacting substance of 220 kDa" encoded by a nucleic acid that hybridizes to the "KIAA1250, homolog of rat kinase D-interacting substance of 220 kDa" nucleic acid or its complement under low stringency conditions, and/or

(xxx) "LPHH1" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LPHH1" encoded by a nucleic acid that hybridizes to the "LPHH1" nucleic acid or its complement under low stringency conditions, and/or

(xxxi) "Lamezin/FKRP" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Lamezin/FKRP" encoded by a nucleic acid that hybridizes to the "Lamezin/FKRP" nucleic acid or its complement under low stringency conditions, and/or

(xxxii) "Laminin, gamma 1 " (SEQ ID No:88) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Laminin, gamma 1 " encoded by a nucleic acid that hybridizes to the "Laminin, gamma 1 " nucleic acid or its complement under low stringency conditions, and/or

(xxxiii) "MAGEB4" (SEQ ID No:223) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MAGEB4" encoded by a nucleic acid that hybridizes to the "MAGEB4" nucleic acid or its complement under low stringency conditions, and/or

(xxxiv) "MGC5442" (SEQ ID No:224) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442"

encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions, and/or

(xxxv) "Neural cell adhesion molecule L1 " (SEQ ID No:225) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neural cell adhesion molecule L1 " encoded by a nucleic acid that hybridizes to the "Neural cell adhesion molecule L1 " nucleic acid or its complement under low stringency conditions, and/or

(xxxvi) "Neurotrypsin" (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions, and/or

(xxxvii) "Nuclear protein SDK3" (SEQ ID No:226) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nuclear protein SDK3" encoded by a nucleic acid that hybridizes to the "Nuclear protein SDK3" nucleic acid or its complement under low stringency conditions, and/or

(xxxviii) "PPIB" (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPIB" encoded by a nucleic acid that hybridizes to the "PPIB" nucleic acid or its complement under low stringency conditions, and/or

(xxxix) "PTDSS1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PTDSS1" encoded by a nucleic acid that hybridizes to the "PTDSS1" nucleic acid or its complement under low stringency conditions, and/or

(xli) "Presenilin1 " (SEQ ID No:123) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin1 " encoded by a nucleic acid that hybridizes to the "Presenilin1 " nucleic acid or its complement under low stringency conditions, and/or

(xlii) "Reelin" (SEQ ID No:97) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Reelin" encoded by a nucleic acid that hybridizes to the "Reelin" nucleic acid or its complement under low stringency conditions, and/or

(xlii) "SCG2" (SEQ ID No:229) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SCG2" encoded by a

nucleic acid that hybridizes to the "SCG2" nucleic acid or its complement under low stringency conditions, and/or

(xlvi) "SIMILAR TO HYPOTHETICAL PROTEIN SB153" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO HYPOTHETICAL PROTEIN SB153" encoded by a nucleic acid that hybridizes to the "SIMILAR TO HYPOTHETICAL PROTEIN SB153" nucleic acid or its complement under low stringency conditions, and/or

(xlv) "STR A6 isoform 1" (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STR A6 isoform 1" encoded by a nucleic acid that hybridizes to the "STR A6 isoform 1" nucleic acid or its complement under low stringency conditions, and/or

(xlv) "Similar to RIKEN cDNA 1100001L14 gene (Fragment)" (SEQ ID No:232) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to RIKEN cDNA 1100001L14 gene (Fragment)" encoded by a nucleic acid that hybridizes to the "Similar to RIKEN cDNA 1100001L14 gene (Fragment)" nucleic acid or its complement under low stringency conditions, and/or

(xlvii) "TLOC1" (SEQ ID No:233) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TLOC1" encoded by a nucleic acid that hybridizes to the "TLOC1" nucleic acid or its complement under low stringency conditions, and/or

(xlviii) "UGCGL2" (SEQ ID No:102) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "UGCGL2" encoded by a nucleic acid that hybridizes to the "UGCGL2" nucleic acid or its complement under low stringency conditions, and/or

(xlix) "VESICULAR INTEGRAL-MEMBRANE PROTEIN VIP36 PRECURSOR" (SEQ ID No:234) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VESICULAR INTEGRAL-MEMBRANE PROTEIN VIP36 PRECURSOR" encoded by a nucleic acid that hybridizes to the "VESICULAR INTEGRAL-MEMBRANE PROTEIN VIP36 PRECURSOR" nucleic acid or its complement under low stringency conditions, and/or

(lx) "Wolframin" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Wolframin" encoded by a nucleic acid that hybridizes to the "Wolframin" nucleic acid or its complement under low stringency conditions, and/or

- (I) "bzw1: basic leucine zipper and w2 domains 1" (SEQ ID No:236) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "bzw1: basic leucine zipper and w2 domains 1" encoded by a nucleic acid that hybridizes to the "bzw1: basic leucine zipper and w2 domains 1" nucleic acid or its complement under low stringency conditions, and/or
- (ii) "dkfzp586c1924" (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "dkfzp586c1924" encoded by a nucleic acid that hybridizes to the "dkfzp586c1924" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "ensp00000258417" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ensp00000258417" encoded by a nucleic acid that hybridizes to the "ensp00000258417" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "hyou1: hypoxia up-regulated 1" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hyou1: hypoxia up-regulated 1" encoded by a nucleic acid that hybridizes to the "hyou1: hypoxia up-regulated 1" nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease, congenital muscular dystrophy 1C and limb-girdle muscular dystrophy 2;.

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease, congenital muscular dystrophy 1C and limb-girdle muscular dystrophy 2;.

34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity,

composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.

37. The method of No. 35, wherein the activity of said complex is determined.

38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

40. The method of No. 39, wherein said determining step comprises determining whether (i) "ASPH" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ASPH" encoded by a

nucleic acid that hybridizes to the "ASPH" nucleic acid or its complement under low stringency conditions, and/or

(ii) "C7orf14" (SEQ ID No:195) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C7orf14" encoded by a nucleic acid that hybridizes to the "C7orf14" nucleic acid or its complement under low stringency conditions, and/or

(iii) "CLNS1A" (SEQ ID No:196) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CLNS1A" encoded by a nucleic acid that hybridizes to the "CLNS1A" nucleic acid or its complement under low stringency conditions, and/or

(iv) "CLU: clusterin (complement lysis inhibitor, SP-40,40, sulfated glycoprotein 2, testosterone-repressed prostate message 2, apolipoprotein J)" (SEQ ID No:197) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CLU: clusterin (complement lysis inhibitor, SP-40,40, sulfated glycoprotein 2, testosterone-repressed prostate message 2, apolipoprotein J)" encoded by a nucleic acid that hybridizes to the "CLU: clusterin (complement lysis inhibitor, SP-40,40, sulfated glycoprotein 2, testosterone-repressed prostate message 2, apolipoprotein J)" nucleic acid or its complement under low stringency conditions, and/or

(v) "CNTNAP1" (SEQ ID No:198) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CNTNAP1" encoded by a nucleic acid that hybridizes to the "CNTNAP1" nucleic acid or its complement under low stringency conditions, and/or

(vi) "COX5B" (SEQ ID No:199) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COX5B" encoded by a nucleic acid that hybridizes to the "COX5B" nucleic acid or its complement under low stringency conditions, and/or

(vii) "COX6B" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COX6B" encoded by a nucleic acid that hybridizes to the "COX6B" nucleic acid or its complement under low stringency conditions, and/or

(viii) "COX6C" (SEQ ID No:201) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COX6C" encoded by a nucleic acid that hybridizes to the "COX6C" nucleic acid or its complement under low stringency conditions, and/or

- (ix) "CSGlcA-T" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CSGlcA-T" encoded by a nucleic acid that hybridizes to the "CSGlcA-T" nucleic acid or its complement under low stringency conditions, and/or
- (x) "DICER1" (SEQ ID No:202) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DICER1" encoded by a nucleic acid that hybridizes to the "DICER1" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "DREV1" (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DREV1" encoded by a nucleic acid that hybridizes to the "DREV1" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "EC 6.3.2.19 (Fragment)" (SEQ ID No:204) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EC 6.3.2.19 (Fragment)" encoded by a nucleic acid that hybridizes to the "EC 6.3.2.19 (Fragment)" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "EIF2B2" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EIF2B2" encoded by a nucleic acid that hybridizes to the "EIF2B2" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "EXTL2" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXTL2" encoded by a nucleic acid that hybridizes to the "EXTL2" nucleic acid or its complement under low stringency conditions, and/or
- (xv) "G2AN" (SEQ ID No:207) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "G2AN" encoded by a nucleic acid that hybridizes to the "G2AN" nucleic acid or its complement under low stringency conditions, and/or
- (xvi) "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" (SEQ ID No:208) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" encoded by a nucleic acid that hybridizes to the "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" nucleic acid or its complement under low stringency conditions, and/or

- (xvii) "HIV-1 Vpr-binding protein (Fragment)" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HIV-1 Vpr-binding protein (Fragment)" encoded by a nucleic acid that hybridizes to the "HIV-1 Vpr-binding protein (Fragment)" nucleic acid or its complement under low stringency conditions, and/or
- (xviii) "HPIP" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HPIP" encoded by a nucleic acid that hybridizes to the "HPIP" nucleic acid or its complement under low stringency conditions, and/or
- (xix) "HSPC329 (Fragment)" (SEQ ID No:211) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC329 (Fragment)" encoded by a nucleic acid that hybridizes to the "HSPC329 (Fragment)" nucleic acid or its complement under low stringency conditions, and/or
- (xx) "HYPOTHETICAL PROTEIN" (SEQ ID No:212) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN" nucleic acid or its complement under low stringency conditions, and/or
- (xxi) "HYPOTHETICAL PROTEIN" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN" nucleic acid or its complement under low stringency conditions, and/or
- (xxii) "HYPOTHETICAL PROTEIN KIAA1524 (FRAGMENT)" (SEQ ID No:214) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN KIAA1524 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN KIAA1524 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or
- (xxiii) "Hypothetical protein FLJ34763" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ34763" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ34763" nucleic acid or its complement under low stringency conditions, and/or

- (xxiv) "Hypothetical protein KIAA0062 (Fragment)" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0062 (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0062 (Fragment)" nucleic acid or its complement under low stringency conditions, and/or
- (xxv) "Hypothetical protein KIAA1500 (Fragment)" (SEQ ID No:217) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA1500 (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA1500 (Fragment)" nucleic acid or its complement under low stringency conditions, and/or
- (xxvi) "IGF2R" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IGF2R" encoded by a nucleic acid that hybridizes to the "IGF2R" nucleic acid or its complement under low stringency conditions, and/or
- (xxvii) "ITGAV" (SEQ ID No:219) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITGAV" encoded by a nucleic acid that hybridizes to the "ITGAV" nucleic acid or its complement under low stringency conditions, and/or
- (xxviii) "ITPR2" (SEQ ID No:220) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITPR2" encoded by a nucleic acid that hybridizes to the "ITPR2" nucleic acid or its complement under low stringency conditions, and/or
- (xxix) "KIAA1250, homolog of rat kinase D-interacting substance of 220 kDa" (SEQ ID No:164) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250, homolog of rat kinase D-interacting substance of 220 kDa" encoded by a nucleic acid that hybridizes to the "KIAA1250, homolog of rat kinase D-interacting substance of 220 kDa" nucleic acid or its complement under low stringency conditions, and/or
- (xxx) "LPHH1" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LPHH1" encoded by a nucleic acid that hybridizes to the "LPHH1" nucleic acid or its complement under low stringency conditions, and/or
- (xxxi) "Lamezin/FKRP" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"Lamezin/FKRP" encoded by a nucleic acid that hybridizes to the "Lamezin/FKRP" nucleic acid or its complement under low stringency conditions, and/or

(xxxii) "Laminin, gamma 1 " (SEQ ID No:88) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Laminin, gamma 1 " encoded by a nucleic acid that hybridizes to the "Laminin, gamma 1 " nucleic acid or its complement under low stringency conditions, and/or

(xxxiii) "MAGEB4" (SEQ ID No:223) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MAGEB4" encoded by a nucleic acid that hybridizes to the "MAGEB4" nucleic acid or its complement under low stringency conditions, and/or

(xxxiv) "MGC5442" (SEQ ID No:224) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions, and/or

(xxxv) "Neural cell adhesion molecule L1 " (SEQ ID No:225) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neural cell adhesion molecule L1 " encoded by a nucleic acid that hybridizes to the "Neural cell adhesion molecule L1 " nucleic acid or its complement under low stringency conditions, and/or

(xxxvi) "Neurotrypsin" (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions, and/or

(xxxvii) "Nuclear protein SDK3" (SEQ ID No:226) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nuclear protein SDK3" encoded by a nucleic acid that hybridizes to the "Nuclear protein SDK3" nucleic acid or its complement under low stringency conditions, and/or

(xxxviii) "PPIB" (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPIB" encoded by a nucleic acid that hybridizes to the "PPIB" nucleic acid or its complement under low stringency conditions, and/or

(xxxix) "PTDSS1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PTDSS1"

encoded by a nucleic acid that hybridizes to the "PTDSS1" nucleic acid or its complement under low stringency conditions, and/or

(xi) "Presenilin1 " (SEQ ID No:123) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin1 " encoded by a nucleic acid that hybridizes to the "Presenilin1 " nucleic acid or its complement under low stringency conditions, and/or

(xii) "Reelin" (SEQ ID No:97) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Reelin" encoded by a nucleic acid that hybridizes to the "Reelin" nucleic acid or its complement under low stringency conditions, and/or

(xiii) "SCG2" (SEQ ID No:229) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SCG2" encoded by a nucleic acid that hybridizes to the "SCG2" nucleic acid or its complement under low stringency conditions, and/or

(xiv) "SIMILAR TO HYPOTHETICAL PROTEIN SB153" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO HYPOTHETICAL PROTEIN SB153" encoded by a nucleic acid that hybridizes to the "SIMILAR TO HYPOTHETICAL PROTEIN SB153" nucleic acid or its complement under low stringency conditions, and/or

(xv) "STRA6 isoform 1" (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STRA6 isoform 1" encoded by a nucleic acid that hybridizes to the "STRA6 isoform 1" nucleic acid or its complement under low stringency conditions, and/or

(xvi) "Similar to RIKEN cDNA 1100001L14 gene (Fragment)" (SEQ ID No:232) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to RIKEN cDNA 1100001L14 gene (Fragment)" encoded by a nucleic acid that hybridizes to the "Similar to RIKEN cDNA 1100001L14 gene (Fragment)" nucleic acid or its complement under low stringency conditions, and/or

(xvii) "TLOC1" (SEQ ID No:233) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TLOC1" encoded by a nucleic acid that hybridizes to the "TLOC1" nucleic acid or its complement under low stringency conditions, and/or

(xviii) "UGCGL2" (SEQ ID No:102) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "UGCGL2"

encoded by a nucleic acid that hybridizes to the "UGCGL2" nucleic acid or its complement under low stringency conditions, and/or

(xlviii) "VESICULAR INTEGRAL-MEMBRANE PROTEIN VIP36 PRECURSOR" (SEQ ID No:234) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VESICULAR INTEGRAL-MEMBRANE PROTEIN VIP36 PRECURSOR" encoded by a nucleic acid that hybridizes to the "VESICULAR INTEGRAL-MEMBRANE PROTEIN VIP36 PRECURSOR" nucleic acid or its complement under low stringency conditions, and/or

(xlix) "Wolframin" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Wolframin" encoded by a nucleic acid that hybridizes to the "Wolframin" nucleic acid or its complement under low stringency conditions, and/or

(I) "bzw1: basic leucine zipper and w2 domains 1" (SEQ ID No:236) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "bzw1: basic leucine zipper and w2 domains 1" encoded by a nucleic acid that hybridizes to the "bzw1: basic leucine zipper and w2 domains 1" nucleic acid or its complement under low stringency conditions, and/or

(II) "dkfp586c1924" (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "dkfp586c1924" encoded by a nucleic acid that hybridizes to the "dkfp586c1924" nucleic acid or its complement under low stringency conditions, and/or

(III) "ensp00000258417" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ensp00000258417" encoded by a nucleic acid that hybridizes to the "ensp00000258417" nucleic acid or its complement under low stringency conditions, and/or

(lvi) "hyou1: hypoxia up-regulated 1" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hyou1: hypoxia up-regulated 1" encoded by a nucleic acid that hybridizes to the "hyou1: hypoxia up-regulated 1" nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative disease such as Alzheimer's disease, congenital muscular dystrophy 1C and limb-girdle muscular dystrophy 2;
42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.
43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.
44. The method according to No. 42 , wherein said disease or disorder involves increased levels of the amount or activity of said complex.
45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins
(i) "ASPH" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ASPH" encoded by a nucleic acid that hybridizes to the "ASPH" nucleic acid or its complement under low stringency conditions,

- (ii) "C7orf14" (SEQ ID No:195) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C7orf14" encoded by a nucleic acid that hybridizes to the "C7orf14" nucleic acid or its complement under low stringency conditions,
- (iii) "CLNS1A" (SEQ ID No:196) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CLNS1A" encoded by a nucleic acid that hybridizes to the "CLNS1A" nucleic acid or its complement under low stringency conditions,
- (iv) "CLU: clusterin (complement lysis inhibitor, SP-40,40, sulfated glycoprotein 2, testosterone-repressed prostate message 2, apolipoprotein J)" (SEQ ID No:197) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CLU: clusterin (complement lysis inhibitor, SP-40,40, sulfated glycoprotein 2, testosterone-repressed prostate message 2, apolipoprotein J)" encoded by a nucleic acid that hybridizes to the "CLU: clusterin (complement lysis inhibitor, SP-40,40, sulfated glycoprotein 2, testosterone-repressed prostate message 2, apolipoprotein J)" nucleic acid or its complement under low stringency conditions,
- (v) "CNTNAP1" (SEQ ID No:198) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CNTNAP1" encoded by a nucleic acid that hybridizes to the "CNTNAP1" nucleic acid or its complement under low stringency conditions,
- (vi) "COX5B" (SEQ ID No:199) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COX5B" encoded by a nucleic acid that hybridizes to the "COX5B" nucleic acid or its complement under low stringency conditions,
- (vii) "COX6B" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COX6B" encoded by a nucleic acid that hybridizes to the "COX6B" nucleic acid or its complement under low stringency conditions,
- (viii) "COX6C" (SEQ ID No:201) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COX6C" encoded by a nucleic acid that hybridizes to the "COX6C" nucleic acid or its complement under low stringency conditions,
- (ix) "CSGlcA-T" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CSGlcA-T"

encoded by a nucleic acid that hybridizes to the "CSGlcA-T" nucleic acid or its complement under low stringency conditions,

(x) "DICER1" (SEQ ID No:202) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DICER1" encoded by a nucleic acid that hybridizes to the "DICER1" nucleic acid or its complement under low stringency conditions,

(xi) "DREV1" (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DREV1" encoded by a nucleic acid that hybridizes to the "DREV1" nucleic acid or its complement under low stringency conditions,

(xii) "EC 6.3.2.19 (Fragment)" (SEQ ID No:204) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EC 6.3.2.19 (Fragment)" encoded by a nucleic acid that hybridizes to the "EC 6.3.2.19 (Fragment)" nucleic acid or its complement under low stringency conditions,

(xiii) "EIF2B2" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EIF2B2" encoded by a nucleic acid that hybridizes to the "EIF2B2" nucleic acid or its complement under low stringency conditions,

(xiv) "EXTL2" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXTL2" encoded by a nucleic acid that hybridizes to the "EXTL2" nucleic acid or its complement under low stringency conditions,

(xv) "G2AN" (SEQ ID No:207) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "G2AN" encoded by a nucleic acid that hybridizes to the "G2AN" nucleic acid or its complement under low stringency conditions,

(xvi) "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" (SEQ ID No:208) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" encoded by a nucleic acid that hybridizes to the "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" nucleic acid or its complement under low stringency conditions,

(xvii) "HIV-1 Vpr-binding protein (Fragment)" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a

variant of "HIV-1 Vpr-binding protein (Fragment)" encoded by a nucleic acid that hybridizes to the "HIV-1 Vpr-binding protein (Fragment)" nucleic acid or its complement under low stringency conditions,

(xvii) "HPIP" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HPIP" encoded by a nucleic acid that hybridizes to the "HPIP" nucleic acid or its complement under low stringency conditions,

(xix) "HSPC329 (Fragment)" (SEQ ID No:211) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC329 (Fragment)" encoded by a nucleic acid that hybridizes to the "HSPC329 (Fragment)" nucleic acid or its complement under low stringency conditions,

(xx) "HYPOTHETICAL PROTEIN" (SEQ ID No:212) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN" nucleic acid or its complement under low stringency conditions,

(xxi) "HYPOTHETICAL PROTEIN" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN" nucleic acid or its complement under low stringency conditions,

(xxii) "HYPOTHETICAL PROTEIN KIAA1524 (FRAGMENT)" (SEQ ID No:214) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN KIAA1524 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN KIAA1524 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xxiii) "Hypothetical protein FLJ34763" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ34763" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ34763" nucleic acid or its complement under low stringency conditions,

(xxiv) "Hypothetical protein KIAA0062 (Fragment)" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0062 (Fragment)" encoded by a nucleic acid

that hybridizes to the "Hypothetical protein KIAA0062 (Fragment)" nucleic acid or its complement under low stringency conditions,

(xxv) "Hypothetical protein KIAA1500 (Fragment)" (SEQ ID No:217) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA1500 (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA1500 (Fragment)" nucleic acid or its complement under low stringency conditions,

(xxvi) "IGF2R" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IGF2R" encoded by a nucleic acid that hybridizes to the "IGF2R" nucleic acid or its complement under low stringency conditions,

(xxvii) "ITGAV" (SEQ ID No:219) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITGAV" encoded by a nucleic acid that hybridizes to the "ITGAV" nucleic acid or its complement under low stringency conditions,

(xxviii) "ITPR2" (SEQ ID No:220) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITPR2" encoded by a nucleic acid that hybridizes to the "ITPR2" nucleic acid or its complement under low stringency conditions,

(xxix) "KIAA1250, homolog of rat kinase D-interacting substance of 220 kDa" (SEQ ID No:164) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250, homolog of rat kinase D-interacting substance of 220 kDa" encoded by a nucleic acid that hybridizes to the "KIAA1250, homolog of rat kinase D-interacting substance of 220 kDa" nucleic acid or its complement under low stringency conditions,

(xxx) "LPHH1" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LPHH1" encoded by a nucleic acid that hybridizes to the "LPHH1" nucleic acid or its complement under low stringency conditions,

(xxxi) "Lamezin/FKRP" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Lamezin/FKRP" encoded by a nucleic acid that hybridizes to the "Lamezin/FKRP" nucleic acid or its complement under low stringency conditions,

- (xxxii) "Laminin, gamma 1 " (SEQ ID No:88) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Laminin, gamma 1 " encoded by a nucleic acid that hybridizes to the "Laminin, gamma 1 " nucleic acid or its complement under low stringency conditions,
- (xxxiii) "MAGEB4" (SEQ ID No:223) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MAGEB4" encoded by a nucleic acid that hybridizes to the "MAGEB4" nucleic acid or its complement under low stringency conditions,
- (xxxiv) "MGC5442" (SEQ ID No:224) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,
- (xxxv) "Neural cell adhesion molecule L1 " (SEQ ID No:225) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neural cell adhesion molecule L1 " encoded by a nucleic acid that hybridizes to the "Neural cell adhesion molecule L1 " nucleic acid or its complement under low stringency conditions,
- (xxxvi) "Neurotrypsin" (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,
- (xxxvii) "Nuclear protein SDK3" (SEQ ID No:226) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nuclear protein SDK3" encoded by a nucleic acid that hybridizes to the "Nuclear protein SDK3" nucleic acid or its complement under low stringency conditions,
- (xxxviii) "PPIB" (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPIB" encoded by a nucleic acid that hybridizes to the "PPIB" nucleic acid or its complement under low stringency conditions,
- (xxxix) "PTDSS1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PTDSS1" encoded by a nucleic acid that hybridizes to the "PTDSS1" nucleic acid or its complement under low stringency conditions,

- (xli) "Presenilin1 " (SEQ ID No:123) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin1 " encoded by a nucleic acid that hybridizes to the "Presenilin1 " nucleic acid or its complement under low stringency conditions,
- (xlii) "Reelin" (SEQ ID No:97) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Reelin" encoded by a nucleic acid that hybridizes to the "Reelin" nucleic acid or its complement under low stringency conditions,
- (xlii) "SCG2" (SEQ ID No:229) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SCG2" encoded by a nucleic acid that hybridizes to the "SCG2" nucleic acid or its complement under low stringency conditions,
- (xliii) "SIMILAR TO HYPOTHETICAL PROTEIN SB153" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO HYPOTHETICAL PROTEIN SB153" encoded by a nucleic acid that hybridizes to the "SIMILAR TO HYPOTHETICAL PROTEIN SB153" nucleic acid or its complement under low stringency conditions,
- (xliv) "STRA6 isoform 1" (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STRA6 isoform 1" encoded by a nucleic acid that hybridizes to the "STRA6 isoform 1" nucleic acid or its complement under low stringency conditions,
- (xlv) "Similar to RIKEN cDNA 1100001L14 gene (Fragment)" (SEQ ID No:232) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to RIKEN cDNA 1100001L14 gene (Fragment)" encoded by a nucleic acid that hybridizes to the "Similar to RIKEN cDNA 1100001L14 gene (Fragment)" nucleic acid or its complement under low stringency conditions,
- (xlvi) "TLOC1" (SEQ ID No:233) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TLOC1" encoded by a nucleic acid that hybridizes to the "TLOC1" nucleic acid or its complement under low stringency conditions,
- (xlvii) "UGCGL2" (SEQ ID No:102) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "UGCGL2" encoded by a nucleic acid that hybridizes to the "UGCGL2" nucleic acid or its complement under low stringency conditions,

(xlviii) "VESICULAR INTEGRAL-MEMBRANE PROTEIN VIP36 PRECURSOR" (SEQ ID No:234) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VESICULAR INTEGRAL-MEMBRANE PROTEIN VIP36 PRECURSOR" encoded by a nucleic acid that hybridizes to the "VESICULAR INTEGRAL-MEMBRANE PROTEIN VIP36 PRECURSOR" nucleic acid or its complement under low stringency conditions,

(xlix) "Wolframin" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Wolframin" encoded by a nucleic acid that hybridizes to the "Wolframin" nucleic acid or its complement under low stringency conditions,

(I) "bzw1: basic leucine zipper and w2 domains 1" (SEQ ID No:236) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "bzw1: basic leucine zipper and w2 domains 1" encoded by a nucleic acid that hybridizes to the "bzw1: basic leucine zipper and w2 domains 1" nucleic acid or its complement under low stringency conditions,

(II) "dkfp586c1924" (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "dkfp586c1924" encoded by a nucleic acid that hybridizes to the "dkfp586c1924" nucleic acid or its complement under low stringency conditions,

(III) "ensp00000258417" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ensp00000258417" encoded by a nucleic acid that hybridizes to the "ensp00000258417" nucleic acid or its complement under low stringency conditions, and/or(III) "hyou1: hypoxia up-regulated 1" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hyou1: hypoxia up-regulated 1" encoded by a nucleic acid that hybridizes to the "hyou1: hypoxia up-regulated 1" nucleic acid or its complement under low stringency conditions, as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease, congenital muscular dystrophy 1C and limb-girdle muscular dystrophy 2;.

The present invention further relates to the following embodiments of the APP-C59-complex

1. A protein complex selected from complex (I) and comprising
 - (a) at least one first protein selected from the group consisting of:
 - (i) "C59" (SEQ ID No:239) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C59" encoded by a nucleic acid that hybridizes to the "C59" nucleic acid or its complement under low stringency conditions,
 - (ii) "Fe65" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
 - (iii) "Fe65L1" (SEQ ID No:242) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions,
 - (iv) "TIP60" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TIP60" encoded by a nucleic acid that hybridizes to the "TIP60" nucleic acid or its complement under low stringency conditions, and
 - (v) "X11beta" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, and
 - (b) at least one second protein, which second protein is selected from the group consisting of:
 - (i) "COPS3" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPS3" encoded by a nucleic acid that hybridizes to the "COPS3" nucleic acid or its complement under low stringency conditions,
 - (ii) "CPNE7" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CPNE7" encoded by a

nucleic acid that hybridizes to the "CPNE7" nucleic acid or its complement under low stringency conditions,

(iii) "CUL3" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CUL3" encoded by a nucleic acid that hybridizes to the "CUL3" nucleic acid or its complement under low stringency conditions,

(iv) "Copine III" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Copine III" encoded by a nucleic acid that hybridizes to the "Copine III" nucleic acid or its complement under low stringency conditions,

(v) "GTF3C3" (SEQ ID No:243) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTF3C3" encoded by a nucleic acid that hybridizes to the "GTF3C3" nucleic acid or its complement under low stringency conditions,

(vi) "NRD1" (SEQ ID No:244) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NRD1" encoded by a nucleic acid that hybridizes to the "NRD1" nucleic acid or its complement under low stringency conditions,

(vii) "S100 beta" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S100 beta" encoded by a nucleic acid that hybridizes to the "S100 beta" nucleic acid or its complement under low stringency conditions, and

(viii) "USP11" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "USP11" encoded by a nucleic acid that hybridizes to the "USP11" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

2. The protein complex according to No. 1 wherein the first protein is the protein C59 (SEQ ID NO. 239), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of 'C59' encoded by a nucleic acid that hybridizes to the 'C59' under low stringency conditions.

3. The protein complex according to No. 1 selected from complex (I) and comprising the following proteins:

- (i) "C59" (SEQ ID No:239) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C59" encoded by a nucleic acid that hybridizes to the "C59" nucleic acid or its complement under low stringency conditions,
- (ii) "COPS3" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPS3" encoded by a nucleic acid that hybridizes to the "COPS3" nucleic acid or its complement under low stringency conditions,
- (iii) "CPNE7" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CPNE7" encoded by a nucleic acid that hybridizes to the "CPNE7" nucleic acid or its complement under low stringency conditions,
- (iv) "CUL3" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CUL3" encoded by a nucleic acid that hybridizes to the "CUL3" nucleic acid or its complement under low stringency conditions,
- (v) "Copine III" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Copine III" encoded by a nucleic acid that hybridizes to the "Copine III" nucleic acid or its complement under low stringency conditions,
- (vi) "Fe65" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
- (vii) "Fe65L1" (SEQ ID No:242) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1"

encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions,

(viii) "GTF3C3" (SEQ ID No:243) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTF3C3" encoded by a nucleic acid that hybridizes to the "GTF3C3" nucleic acid or its complement under low stringency conditions,

(ix) "NRD1" (SEQ ID No:244) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NRD1" encoded by a nucleic acid that hybridizes to the "NRD1" nucleic acid or its complement under low stringency conditions,

(x) "S100 beta" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S100 beta" encoded by a nucleic acid that hybridizes to the "S100 beta" nucleic acid or its complement under low stringency conditions,

(xi) "TIP60" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TIP60" encoded by a nucleic acid that hybridizes to the "TIP60" nucleic acid or its complement under low stringency conditions,

(xii) "USP11" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "USP11" encoded by a nucleic acid that hybridizes to the "USP11" nucleic acid or its complement under low stringency conditions, and/or

(xiii) "X11beta" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 7 of the following proteins:

(i) "C59" (SEQ ID No:239) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C59" encoded by a nucleic acid that hybridizes to the "C59" nucleic acid or its complement under low stringency conditions,

- (ii) "COPS3" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPS3" encoded by a nucleic acid that hybridizes to the "COPS3" nucleic acid or its complement under low stringency conditions,
- (iii) "CPNE7" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CPNE7" encoded by a nucleic acid that hybridizes to the "CPNE7" nucleic acid or its complement under low stringency conditions,
- (iv) "CUL3" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CUL3" encoded by a nucleic acid that hybridizes to the "CUL3" nucleic acid or its complement under low stringency conditions,
- (v) "Copine III" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Copine III" encoded by a nucleic acid that hybridizes to the "Copine III" nucleic acid or its complement under low stringency conditions,
- (vi) "Fe65" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
- (vii) "Fe65L1" (SEQ ID No:242) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions,
- (viii) "GTF3C3" (SEQ ID No:243) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTF3C3" encoded by a nucleic acid that hybridizes to the "GTF3C3" nucleic acid or its complement under low stringency conditions,
- (ix) "NRD1" (SEQ ID No:244) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NRD1" encoded by a nucleic acid that hybridizes to the "NRD1" nucleic acid or its complement under low stringency conditions,
- (x) "S100 beta" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S100 beta"

encoded by a nucleic acid that hybridizes to the "S100 beta" nucleic acid or its complement under low stringency conditions,

(xi) "TIP60" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TIP60" encoded by a nucleic acid that hybridizes to the "TIP60" nucleic acid or its complement under low stringency conditions,

(xii) "USP11" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "USP11" encoded by a nucleic acid that hybridizes to the "USP11" nucleic acid or its complement under low stringency conditions,

(xiii) "X11beta" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.

6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.

7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.

8. The complex of any of No. 1 - 7 that is involved in the transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).

9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps: expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.
10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.
11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.
12. Component of the APP-C59/AICD complex obtainable by a process according to any of No. 9 - 11.
13. Protein of the APP-C59/AICD complex selected from
- (i) "CPNE7" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CPNE7" encoded by a nucleic acid that hybridizes to the "CPNE7" nucleic acid or its complement under low stringency conditions, and
 - (ii) "Copine III" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Copine III" encoded by a nucleic acid that hybridizes to the "Copine III" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.
14. Nucleic acid encoding a protein according to No. 13.

15. Construct, preferably a vector construct, comprising (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or
(b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).

16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).

17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.

18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.

19. The kit according to No. 18 for processing a substrate of said complex.

20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; .

21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.

22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.

23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:

(i) "CPNE7" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CPNE7" encoded by a nucleic acid that hybridizes to the "CPNE7" nucleic acid or its complement under low stringency conditions, and/or

(ii) "Copine III" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Copine III" encoded by a nucleic acid that hybridizes to the "Copine III" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative disease such as Alzheimer's disease; .

25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:

(i) "CPNE7" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CPNE7" encoded by a nucleic acid that hybridizes to the "CPNE7" nucleic acid or its complement under low stringency conditions, and/or

(ii) "Copine III" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Copine III"

encoded by a nucleic acid that hybridizes to the "Copine III" nucleic acid or its complement under low stringency conditions, comprising the steps of

- (a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and
- (b) determining whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of (a) exposing said complex, or a cell or organism containing APP-C59/AICD complex to one or more candidate molecules; and

(b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.

28. The method of No. 26, wherein the activity of said complex is determined.

29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.

30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.

31. The method of No. 30, wherein said determining step comprises determining whether

- (i) "C59" (SEQ ID No:239) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C59" encoded by a nucleic acid that hybridizes to the "C59" nucleic acid or its complement under low stringency conditions, and/or
- (ii) "COPS3" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPS3" encoded by a nucleic acid that hybridizes to the "COPS3" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "CPNE7" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CPNE7" encoded by a nucleic acid that hybridizes to the "CPNE7" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "CUL3" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CUL3" encoded by a nucleic acid that hybridizes to the "CUL3" nucleic acid or its complement under low stringency conditions, and/or
- (v) "Copine III" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Copine III" encoded by a nucleic acid that hybridizes to the "Copine III" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "Fe65" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "Fe65L1" (SEQ ID No:242) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "GTF3C3" (SEQ ID No:243) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTF3C3"

encoded by a nucleic acid that hybridizes to the "GTF3C3" nucleic acid or its complement under low stringency conditions, and/or

(ix) "NRD1" (SEQ ID No:244) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NRD1" encoded by a nucleic acid that hybridizes to the "NRD1" nucleic acid or its complement under low stringency conditions, and/or

(x) "S100 beta" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S100 beta" encoded by a nucleic acid that hybridizes to the "S100 beta" nucleic acid or its complement under low stringency conditions, and/or

(xi) "TIP60" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TIP60" encoded by a nucleic acid that hybridizes to the "TIP60" nucleic acid or its complement under low stringency conditions, and/or

(xii) "USP11" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "USP11" encoded by a nucleic acid that hybridizes to the "USP11" nucleic acid or its complement under low stringency conditions, and/or

(xiii) "X11beta" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; .

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; .

34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity,

composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.

37. The method of No. 35, wherein the activity of said complex is determined.

38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

40. The method of No. 39, wherein said determining step comprises determining whether (i) "C59" (SEQ ID No:239) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C59" encoded by a nucleic

acid that hybridizes to the "C59" nucleic acid or its complement under low stringency conditions, and/or

(ii) "COPS3" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPS3" encoded by a nucleic acid that hybridizes to the "COPS3" nucleic acid or its complement under low stringency conditions, and/or

(iii) "CPNE7" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CPNE7" encoded by a nucleic acid that hybridizes to the "CPNE7" nucleic acid or its complement under low stringency conditions, and/or

(iv) "CUL3" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CUL3" encoded by a nucleic acid that hybridizes to the "CUL3" nucleic acid or its complement under low stringency conditions, and/or

(v) "Copine III" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Copine III" encoded by a nucleic acid that hybridizes to the "Copine III" nucleic acid or its complement under low stringency conditions, and/or

(vi) "Fe65" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions, and/or

(vii) "Fe65L1" (SEQ ID No:242) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions, and/or

(viii) "GTF3C3" (SEQ ID No:243) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTF3C3" encoded by a nucleic acid that hybridizes to the "GTF3C3" nucleic acid or its complement under low stringency conditions, and/or

(ix) "NRD1" (SEQ ID No:244) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NRD1" encoded by a nucleic acid that hybridizes to the "NRD1" nucleic acid or its complement under low stringency conditions, and/or

- (x) "S100 beta" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S100 beta" encoded by a nucleic acid that hybridizes to the "S100 beta" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "TIP60" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TIP60" encoded by a nucleic acid that hybridizes to the "TIP60" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "USP11" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "USP11" encoded by a nucleic acid that hybridizes to the "USP11" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "X11beta" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; .

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42 , wherein said disease or disorder involves increased levels of the amount or activity of said complex.

45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins

- (i) "C59" (SEQ ID No:239) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C59" encoded by a nucleic acid that hybridizes to the "C59" nucleic acid or its complement under low stringency conditions,
- (ii) "COPS3" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPS3" encoded by a nucleic acid that hybridizes to the "COPS3" nucleic acid or its complement under low stringency conditions,
- (iii) "CPNE7" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CPNE7" encoded by a nucleic acid that hybridizes to the "CPNE7" nucleic acid or its complement under low stringency conditions,
- (iv) "CUL3" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CUL3" encoded by a nucleic acid that hybridizes to the "CUL3" nucleic acid or its complement under low stringency conditions,
- (v) "Copine III" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Copine III" encoded by a nucleic acid that hybridizes to the "Copine III" nucleic acid or its complement under low stringency conditions,
- (vi) "Fe65" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
- (vii) "Fe65L1" (SEQ ID No:242) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions,
- (viii) "GTF3C3" (SEQ ID No:243) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTF3C3"

encoded by a nucleic acid that hybridizes to the "GTF3C3" nucleic acid or its complement under low stringency conditions,

(ix) "NRD1" (SEQ ID No:244) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NRD1" encoded by a nucleic acid that hybridizes to the "NRD1" nucleic acid or its complement under low stringency conditions,

(x) "S100 beta" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S100 beta" encoded by a nucleic acid that hybridizes to the "S100 beta" nucleic acid or its complement under low stringency conditions,

(xi) "TIP60" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TIP60" encoded by a nucleic acid that hybridizes to the "TIP60" nucleic acid or its complement under low stringency conditions,

(xii) "USP11" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "USP11" encoded by a nucleic acid that hybridizes to the "USP11" nucleic acid or its complement under low stringency conditions, and/or(xiii) "X11beta" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions,as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; .

The invention further relates to the following embodiments of the BRI-complex

1. A protein complex selected from complex (I) and comprising

(a) at least one first protein selected from the group consisting of:

(i) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:249) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions, and

(b) at least one second protein, which second protein is selected from the group consisting of:

- (i) "APLP2" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,
- (ii) "APP" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (iii) "CARBOXYPEPTIDASE D" (SEQ ID No:246) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CARBOXYPEPTIDASE D" encoded by a nucleic acid that hybridizes to the "CARBOXYPEPTIDASE D" nucleic acid or its complement under low stringency conditions,
- (iv) "Contactin1" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Contactin1" encoded by a nucleic acid that hybridizes to the "Contactin1" nucleic acid or its complement under low stringency conditions,
- (v) "DPP6 (DIPEPTIDYL AMINOPEPTIDASE-LIKE PROTEIN 6)" (SEQ ID No:247) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DPP6 (DIPEPTIDYL AMINOPEPTIDASE-LIKE PROTEIN 6)" encoded by a nucleic acid that hybridizes to the "DPP6 (DIPEPTIDYL AMINOPEPTIDASE-LIKE PROTEIN 6)" nucleic acid or its complement under low stringency conditions, and
- (vi) "Delta-like homolog" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-like homolog" encoded by a nucleic acid that hybridizes to the "Delta-like homolog" nucleic acid or its complement under low stringency conditions, and
- (vii) "ITM2C" (SEQ ID No:248) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITM2C" encoded by a nucleic acid that hybridizes to the "ITM2C" nucleic acid or its complement under low stringency conditions

and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

2. The protein complex according to No. 1 wherein the first protein is the protein ITM2B (SEQ ID NO. 249), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of 'ITM2B' encoded by a nucleic acid that hybridizes to the 'ITM2B' under low stringency conditions.

3. The protein complex according to No. 1 selected from complex (I) and comprising the following proteins:

- (i) "APLP2" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,
- (ii) "APP" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (iii) "CARBOXYPEPTIDASE D" (SEQ ID No:246) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CARBOXYPEPTIDASE D" encoded by a nucleic acid that hybridizes to the "CARBOXYPEPTIDASE D" nucleic acid or its complement under low stringency conditions,
- (iv) "Contactin1" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Contactin1" encoded by a nucleic acid that hybridizes to the "Contactin1" nucleic acid or its complement under low stringency conditions,

- (v) "DPP6 (DIPEPTIDYL AMINOPEPTIDASE-LIKE PROTEIN 6)" (SEQ ID No:247) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DPP6 (DIPEPTIDYL AMINOPEPTIDASE-LIKE PROTEIN 6)" encoded by a nucleic acid that hybridizes to the "DPP6 (DIPEPTIDYL AMINOPEPTIDASE-LIKE PROTEIN 6)" nucleic acid or its complement under low stringency conditions,
- (vi) "Delta-like homolog" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-like homolog" encoded by a nucleic acid that hybridizes to the "Delta-like homolog" nucleic acid or its complement under low stringency conditions,
- (vii) "ITM2C" (SEQ ID No:248) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITM2C" encoded by a nucleic acid that hybridizes to the "ITM2C" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:249) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,
- and a protein complex selected from complex (II) and comprising the following proteins:
- (i) "APLP2" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,
- (ii) "APP" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (iii) "CARBOXYPEPTIDASE D" (SEQ ID No:246) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CARBOXYPEPTIDASE D" encoded by a nucleic acid that hybridizes to the "CARBOXYPEPTIDASE D" nucleic acid or its complement under low stringency conditions,

- (iv) "Contactin1" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Contactin1" encoded by a nucleic acid that hybridizes to the "Contactin1" nucleic acid or its complement under low stringency conditions,
- (v) "DPP6 (DIPEPTIDYL AMINOPEPTIDASE-LIKE PROTEIN 6)" (SEQ ID No:247) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DPP6 (DIPEPTIDYL AMINOPEPTIDASE-LIKE PROTEIN 6)" encoded by a nucleic acid that hybridizes to the "DPP6 (DIPEPTIDYL AMINOPEPTIDASE-LIKE PROTEIN 6)" nucleic acid or its complement under low stringency conditions,
- (vi) "Delta-like homolog" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-like homolog" encoded by a nucleic acid that hybridizes to the "Delta-like homolog" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:249) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,
- and a protein complex selected from complex (III) and comprising the following proteins:
- (i) "APLP2" (SEQ ID No:4) or a functionally active derivative thereof,
 - (ii) "APP" (SEQ ID No:5) or a functionally active derivative thereof,
 - (iii) "CARBOXYPEPTIDASE D" (SEQ ID No:246) or a functionally active derivative thereof,
 - (iv) "Contactin1" (SEQ ID No:12) or a functionally active derivative thereof,
 - (v) "DPP6 (DIPEPTIDYL AMINOPEPTIDASE-LIKE PROTEIN 6)" (SEQ ID No:247) or a functionally active derivative thereof,
 - (vi) "Delta-like homolog" (SEQ ID No:160) or a functionally active derivative thereof,
 - (vii) "ITM2C" (SEQ ID No:248) or a functionally active derivative thereof, and
 - (viii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:249) or a functionally active derivative thereof,

4. The protein complex according to No. 1 comprising all but 1 - 5 of the following proteins:

- (i) "APLP2" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,
- (ii) "APP" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (iii) "CARBOXYPEPTIDASE D" (SEQ ID No:246) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CARBOXYPEPTIDASE D" encoded by a nucleic acid that hybridizes to the "CARBOXYPEPTIDASE D" nucleic acid or its complement under low stringency conditions,
- (iv) "Contactin1" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Contactin1" encoded by a nucleic acid that hybridizes to the "Contactin1" nucleic acid or its complement under low stringency conditions,
- (v) "DPP6 (DIPEPTIDYL AMINOPEPTIDASE-LIKE PROTEIN 6)" (SEQ ID No:247) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DPP6 (DIPEPTIDYL AMINOPEPTIDASE-LIKE PROTEIN 6)" encoded by a nucleic acid that hybridizes to the "DPP6 (DIPEPTIDYL AMINOPEPTIDASE-LIKE PROTEIN 6)" nucleic acid or its complement under low stringency conditions,
- (vi) "Delta-like homolog" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-like homolog" encoded by a nucleic acid that hybridizes to the "Delta-like homolog" nucleic acid or its complement under low stringency conditions,
- (vii) "ITM2C" (SEQ ID No:248) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITM2C" encoded by a nucleic acid that hybridizes to the "ITM2C" nucleic acid or its complement under low stringency conditions,
- (viii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:249) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that

hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.
6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.
7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.
8. The complex of any of No. 1 - 7 that is involved in the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).
9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps: expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is

attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.

10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.

11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.

12. Component of the BRI/ITM2B complex obtainable by a process according to any of No. 9 - 11.

13. Construct, preferably a vector construct, comprising at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative thereof at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1(a) and at least one of said proteins, or functionally active fragments of functionally active derivative thereof being selected from the second group of proteins according to No. 1(b).

14. Host cell containing a construct of No. 13 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).

15. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. .

16. A kit comprising in one or more container the complex of any of No. 1 - 8 optionally together with an antibody according to No. 15 and/or further components such as reagents and working instructions.
17. The kit according to No. 16 for processing a substrate of said complex.
18. The kit according to No. 16 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative disease such as Alzheimer's disease and familial British dementia; .
19. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one antibody according to No. 15 is attached to a solid carrier.
20. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.
21. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8..
22. A pharmaceutical composition according to No. 21 for the treatment of diseases and disorders such as neurodegenerative disease such as Alzheimer's disease and familial British dementia; .
23. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8. comprising the steps of
 - (a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and
 - (b) determinig whether said candidate molecule is bound to the complex or protein.
24. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of(a) exposing said complex, or a cell or organism containing BRI/ITM2B complex to one or more candidate molecules; and

(b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

25. The method of No. 24, wherein the amount of said complex is determined.

26. The method of No. 24, wherein the activity of said complex is determined.

27. The method of No. 26, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.

28. The method of No. 24, wherein the amount of the individual protein components of said complex are determined.

29. The method of No. 28, wherein said determining step comprises determining whether
(i) "APLP2" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions, and/or

(ii) "APP" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or

- (iii) "CARBOXYPEPTIDASE D" (SEQ ID No:246) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CARBOXYPEPTIDASE D" encoded by a nucleic acid that hybridizes to the "CARBOXYPEPTIDASE D" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "Contactin1" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Contactin1" encoded by a nucleic acid that hybridizes to the "Contactin1" nucleic acid or its complement under low stringency conditions, and/or
- (v) "DPP6 (DIPEPTIDYL AMINOPEPTIDASE-LIKE PROTEIN 6)" (SEQ ID No:247) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DPP6 (DIPEPTIDYL AMINOPEPTIDASE-LIKE PROTEIN 6)" encoded by a nucleic acid that hybridizes to the "DPP6 (DIPEPTIDYL AMINOPEPTIDASE-LIKE PROTEIN 6)" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "Delta-like homolog" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-like homolog" encoded by a nucleic acid that hybridizes to the "Delta-like homolog" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "ITM2C" (SEQ ID No:248) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITM2C" encoded by a nucleic acid that hybridizes to the "ITM2C" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:249) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions, is present in the complex.

30. The method of any of No. 24 - 29, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease and familial British dementia; .

31. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease and familial British dementia; .

32. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

33. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

34. The method of No. 33, wherein the amount of said complex is determined.

35. The method of No. 33, wherein the activity of said complex is determined.

36. The method of No. 35, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

37. The method of No. 33, wherein the amount of the individual protein components of said complex is determined.

38. The method of No. 37, wherein said determining step comprises determining whether

(i) "APLP2" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions, and/or

(ii) "APP" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or

(iii) "CARBOXYPEPTIDASE D" (SEQ ID No:246) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CARBOXYPEPTIDASE D" encoded by a nucleic acid that hybridizes to the "CARBOXYPEPTIDASE D" nucleic acid or its complement under low stringency conditions, and/or

(iv) "Contactin1" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Contactin1" encoded by a nucleic acid that hybridizes to the "Contactin1" nucleic acid or its complement under low stringency conditions, and/or

(v) "DPP6 (DIPEPTIDYL AMINOPEPTIDASE-LIKE PROTEIN 6)" (SEQ ID No:247) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DPP6 (DIPEPTIDYL AMINOPEPTIDASE-LIKE PROTEIN 6)" encoded by a nucleic acid that hybridizes to the "DPP6 (DIPEPTIDYL AMINOPEPTIDASE-LIKE PROTEIN 6)" nucleic acid or its complement under low stringency conditions, and/or

(vi) "Delta-like homolog" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-like homolog" encoded by a nucleic acid that hybridizes to the "Delta-like homolog" nucleic acid or its complement under low stringency conditions, and/or

(vii) "ITM2C" (SEQ ID No:248) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITM2C" encoded by a

nucleic acid that hybridizes to the "ITM2C" nucleic acid or its complement under low stringency conditions, and/or

(viii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:249) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions, is present in the complex.

39. The complex of any one of No. 1 - 8 or the antibody or fragment of No. 15, for use in a method of diagnosing a disease or disorder such as neurodegenerative disease such as Alzheimer's disease and familial British dementia; .

40. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

41. The method according to No. 40, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

42. The method according to No. 40 , wherein said disease or disorder involves increased levels of the amount or activity of said complex.

43. Complex of any of No. 1 - 8 and/or protein selected from the following proteins

- (i) "APLP2" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,
- (ii) "APP" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (iii) "CARBOXYPEPTIDASE D" (SEQ ID No:246) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CARBOXYPEPTIDASE D" encoded by a nucleic acid that hybridizes to the "CARBOXYPEPTIDASE D" nucleic acid or its complement under low stringency conditions,
- (iv) "Contactin1" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Contactin1" encoded by a nucleic acid that hybridizes to the "Contactin1" nucleic acid or its complement under low stringency conditions,
- (v) "DPP6 (DIPEPTIDYL AMINOPEPTIDASE-LIKE PROTEIN 6)" (SEQ ID No:247) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DPP6 (DIPEPTIDYL AMINOPEPTIDASE-LIKE PROTEIN 6)" encoded by a nucleic acid that hybridizes to the "DPP6 (DIPEPTIDYL AMINOPEPTIDASE-LIKE PROTEIN 6)" nucleic acid or its complement under low stringency conditions,
- (vi) "Delta-like homolog" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-like homolog" encoded by a nucleic acid that hybridizes to the "Delta-like homolog" nucleic acid or its complement under low stringency conditions,
- (vii) "ITM2C" (SEQ ID No:248) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITM2C" encoded by a nucleic acid that hybridizes to the "ITM2C" nucleic acid or its complement under low

stringency conditions, and/or(viii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:249) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions, as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease and familial British dementia; .

5. PROTOCOLS:

The TAP-technology, which is more fully described in EP 1 105 508 B1 and in Rigaut, et al., 1999, Nature Biotechnol. 17:1030-1032 respectively was used and further adapted as described below for protein purification. Proteins were identified using mass spectrometry as described further below.

5.1 Construction of TAP-tagged bait

The cDNAs encoding the complete ORF were obtained by RT-PCR. Total RNA was prepared from appropriate cell lines using the RNeasy Mini Kit (Qiagen). Both cDNA synthesis and PCR were performed with the SUPERSCRIPT One-Step RT-PCR for Long templates Kit (Life Technologies) using gene-specific primers. After 35-40 cycles of amplification PCR-products with the expected size were gel-purified with the MinElute PCR Purification Kit (Qiagen) and, if necessary, used for further amplification. Low-abundant RNAs were amplified by nested PCR before gel-purification. Restriction sites for NotI were attached to PCR primers to allow subcloning of amplified cDNAs into the retroviral vectors pIE94-N/C-TAP thereby generating N- or C-terminal fusions with the TAP-tag (Rigaut et al., 1999, Nature Biotechnol. 17:1030-1032).

N-terminal tagging was chosen for the following baits/entry points: APP-C59, Dab1, PC7, TFCP2, Jip1.

C-terminal tagging was chosen for the following baits/entry points: Bace1, BRI, Fe65L2, Neurotrypsin, Telencephalin, .

Both N- and C-terminal tagging was used for the following baits/entry points: Bace2, p75-NTR, Hunc18a, Lamezin, Pilt, VTRP

Clones were analyzed by restriction digest, DNA sequencing and by in vitro translation using the TNT T7 Quick Coupled Transcription/Translation System (Promega inc.). The presence of the proteins was proven by Western blotting using the protein A part of the TAP-tag for detection. Briefly, separation of proteins by standard SDS-PAGE was followed by semi-dry transfer onto a nitrocellulose membrane (PROTRAN, Schleicher&Schuell) using the MultiphorII blotting apparatus from Pharmacia Biotech. The transfer buffer consisted of 48 mM Tris, 39 mM glycine, 10% methanol and 0,0375% sodium dodecylsulfate. After blocking in phosphate-buffered saline (PBS) supplemented with 10% dry milk powder and 0,1% Tween 20 transferred proteins were probed with the Peroxidase-Anti-Peroxidase Soluble Complex (Sigma) diluted in blocking solution. After intensive washing immunoreactive proteins were visualized by enhanced chemiluminescence (ECL; Amersham Pharmacia Biotech).

5.2 Preparation of Virus and infection

As a vector, a MoMLV-based recombinant virus was used.

The preparation has been carried out as follows:

5.2.1 Preparation of Virus

293 gp cells were grown to 100% confluency. They were split 1:5 on poly-L-Lysine plates (1:5 diluted poly-L-Lysine [0.01% stock solution, Sigma P-4832] in PBS, left on plates for at least 10 min.). On Day 2, 63 microgram of retroviral Vector DNA together with 13 microgram of DNA of plasmid encoding an appropriate envelope protein were transfected into 293 gp cells (Somia, et al., 1999, Proc. Natl. Acad. Sci. USA 96:12667-12672; Somia, et al. 2000, J. Virol. 74:4420-4424). On Day 3, the medium was replaced with 15 ml DMEM + 10% FBS per 15-cm dish. On Day 4, the medium containing viruses (supernatant) was harvested (at 24 h following medium change after transfection). When a second collection was planned, DMEM 10 % FBS was added to the plates and the plates were incubated for another 24 h. All collections were done as follows: The

supernatant was filtered through 0.45 micrometer filter (Corning GmbH, cellulose acetate, 431155). The filter was placed into konical polyallomer centrifuge tubes (Beckman, 358126) that are placed in buckets of a SW 28 rotor (Beckman). The filtered supernatant was ultracentrifuged at 19400 rpm in the SW 28 rotor, for 2 hours at 21 degree Celsius. The supernatant was discarded. The pellet containing viruses was resuspended in a small volume (for example 300 microliter) of Hank's Balanced Salt Solution [Gibco BRL, 14025-092], by pipetting up and down 100-times, using an aerosol-safe tip. The viruses were used for transfection as described below.

5.2.2 Infection

Cells that were infected were plated one day before into one well of a 6-well plate. 4 hours before infection, the old medium on the cells was replaced with fresh medium. Only a minimal volume was added, so that the cells are completely covered (e.g. 700 microliter). During infection, the cells were actively dividing.

A description of the cells and their growth conditions is given in 5.2.3

To the concentrated virus, polybrene (Hexadimethrine Bromide; Sigma, H 9268) was added to achieve a final concentration of 8 microgram/ml (this is equivalent to 2.4 microliter of the 1 milligram/ml polybrene stock per 300 microliter of concentrated retrovirus). The virus was incubated in polybrene at room temperature for 1 hour. For infection, the virus/polybrene mixture was added to the cells and incubated at 37 degree Celsius at the appropriate CO₂ concentration for several hours (e.g. over-day or over-night). Following infection, the medium on the infected cells was replaced with fresh medium. The cells were passaged as usual after they became confluent. The cells contain the retrovirus integrated into their chromosomes and stably express the gene of interest.

5.2.3 Cell lines

The following cell lines were used:

APP-C59-complex: SKN-BE2-cell line; Bace1-complex: SKN-BE2-cell line, HEK-293-cell line, Lan5-cell line; Bace2-complex: SKN-BE2-cell line; BRI-complex: SKN-BE2-cell line; mDab1-complex: SKN-BE2-cell line; Fe65L2-complex: SKN-BE2-cell line; P75-NTR-complex: SKN-BE2-cell line, HEK-293-cell line; Pilt-complex: SKN-BE2-cell line; Paladin-complex: SKN-BE2-cell line, HEK-293-cell line; Neurotrypsin-complex: SKN-BE2-cell line, HEK-293-cell line; Hunc18a-complex: SKN-BE2-cell line, Lan1-cell line; PC7-complex: SKN-BE2-cell line; TFCP2-complex: SKN-BE2-cell line; JIP1-complex: SKN-BE2-cell line, HEK-293-cell line; Lamezin-complex: SKN-BE2-cell line; VTRP-complex: SKN-BE2-cell line

For expression, SKN-BE2 cells were used. SKN-BE2 cells (American Type Culture Collection-No. CRL-2271) were grown in 95% OptiMEM + 5% iron-supplemented calf serum.

LAN-cells (human neuroblastoma cells) were grown in 90% RPMI 1640 + 10% FBS

The expression pattern of the TAP-tagged proteins was checked by immunoblot-analysis as described in 5.3.3 and/or by immunofluorescence as described in 5.3.1 or 5.3.2.

5.3 Checking of expression pattern of TAP-tagged proteins

The expression pattern of the TAP-tagged protein was checked by immunoblot analysis and/or by immunofluorescence. Immunofluorescence analysis was either carried out according to section 5.3.1 or to section 5.3.2 depending on the type of the TAP-tagged protein. Immunoblot analysis was carried out according to section 5.3.3.

5.3.1 Protocol for the indirect Immunofluorescence staining of fixed mammalian cells for plasma membrane and ER bound proteins

Cells were grown in FCS media on polylysine coated 8 well chamber slides to 50% confluency. Then fixation of the cells was performed in 4% ParaFormAldehyde diluted in Phosphate Buffer Saline (PBS) solution (0.14M Phosphate, 0.1M NaCl pH 7.4). The cells were incubated for 30 minutes at room temperature in 300 microliters per well.

Quenching was performed in 0.1M Glycine in PBS for 2x 20 minutes at room temperature. Blocking was performed with 1% Bovine Serum Albumin (BSA) in 0.3% Saponin + PBS for at least 1 hour at room temperature. Incubation of the primary antibodies was performed in the blocking solution overnight at +4°C. The proper dilution of the antibodies was determined in a case to case basis. Cells were washed in PBS containing 0.3% Saponin for 2x 20 minutes at room temperature. Incubation of the secondary antibodies is performed in the blocking solution. Alexa 594 coupled goat anti-rabbit is diluted 1:1000 (Molecular Probes). Alexa 488 coupled goat anti-mouse is diluted 1:1000 (Molecular Probes). DAPI was used to label DNA. If Phalloidin was used to label F-actin, the drug is diluted 1:500 and incubated with the secondary antibodies. Cells were then washed again 2x 20 minutes at room temperature in PBS. The excess of buffer was removed and cells were mounted in a media containing an anti-bleaching agent (Vectashield, Vector Laboratories).

5.3.2 Protocol for the indirect Immunofluorescence staining of fixed mammalian cells for non-plasma membrane bound proteins:

Cells were grown in FCS media on Polylysine coated 8 well chamber slides to 50% confluence. Fixation of the cells was performed in 4% ParaFormAldehyde diluted in Phosphate Buffer Saline (PBS) solution (0.14M Phosphate, 0.1M NaCl pH 7.4) for 30 minutes at Room Temperature (RT), 300 microliters per well. Quenching was performed in 0.1M Glycine in PBS for 2x 20 minutes at room temperature. Permeabilization of cells was done with 0.5% Triton X-100 in PBS for 10 minutes at room temperature. Blocking was then done in 1% Bovine Serum Albumin (BSA) in 0.3% Saponin + PBS for at least 1 hour at RT (Blocking solution). Incubation of the primary antibodies was performed in the blocking solution, overnight at +4°C. The proper dilution of the antibodies has to be determined in a case to case basis. Cells were washed in PBS containing 0.3% Saponin, for 2x 20 minutes at RT. Incubation of the secondary antibodies was performed in the blocking solution. Alexa 594 coupled goat anti-rabbit is diluted 1:1000 (Molecular Probes), Alexa 488 coupled goat anti-mouse is diluted 1:1000 (Molecular Probes). DAPI was used to label DNA. If Phalloidin is used to label F-actin, the drug is diluted 1:500 and incubated with the secondary antibodies. Cells were washed 2x 20 minutes at RT in

PBS. The excess of buffer was removed and cells were mounted in a media containing an anti-bleaching agent (Vectashield, Vector Laboratories).

5.3.3 Immunoblot analysis

To analyze expression levels of TAP-tagged proteins, a cell pellet (from a 6-well dish) was lysed in 60 μ l DNase I buffer (5% Glycerol, 100 mM NaCl, 0.8 % NP-40 (IGEPAL), 5 mM magnesium sulfate, 100 μ g/ml DNase I (Roche Diagnostics), 50 mM Tris, pH 7.5, protease inhibitor cocktail) for 15 min on ice. Each sample was split into two aliquots. The first half was centrifuged at 13,000 rpm for 5 min. to yield the NP-40-extractable material in the supernatant; the second half (total material) was carefully triturated. 50 μ g each of the NP-40-extractable material and the total material are mixed with DTT-containing sample buffer for 30 min at 50°C on a shaker and separated by SDS polyacrylamide gel electrophoresis on a precast 4-12% Bis-Tris gel (Invitrogen). Proteins were then transferred to nitrocellulose using a semi-dry procedure with a discontinuous buffer system. Briefly, gel and nitrocellulose membrane were stacked between filter papers soaked in either anode buffer (three layers buffer A1 (0.3 M Tris-HCl) and three layers buffer A2 (0.03 M Tris-HCl)) or cathode buffer (three layers of 0.03 M Tris-HCl, pH 9.4, 0.1 % SDS, 40 mM ϵ -aminocapronic acid). Electrotransfer of two gels at once was performed at 600 mA for 25 min. Transferred proteins were visualized with Ponceau S solution for one min to control transfer efficiency and then destained in water. The membrane was blocked in 5% non-fat milk powder in TBST (TBS containing 0.05% Tween-20) for 30 min at room temperature. It was subsequently incubated with HRP-coupled PAP antibody (1:5000 diluted in 5% milk/TBST) for 1 h at room temperature, washed three times for 10 min in TBST. The blot membrane was finally soaked in chemiluminescent substrate (ECL, Roche Diagnostics) for 2 min. and either exposed to X-ray film or analyzed on an imaging station.

5.4 Purification of protein complexes

Protein complex purification was adapted to the sub-cellular localization of the TAP-tagged protein and was performed as described below.

5.4.1 Lysate preparation for cytoplasmic proteins

About 1×10^9 adherent cells (average) were harvested with a cell scrapper and washed 3 times in ice-cold PBS (3 min, 550g). Collected cells were frozen in liquid nitrogen or immediately processed further. For cell lysis, the cell pellet was resuspended in 10 ml of CZ lysis buffer (50 mM Tris-Cl, pH 7.4; 5 % Glycerol; 0,2 % IGEPAL; 1.5 mM MgCl₂; 100 mM NaCl; 25 mM NaF; 1 mM Na₃VO₄; 1 mM DTT; containing 1 tablet of EDTA-free Protease inhibitor cocktail (Complete™, Roche) per 25 ml of buffer) and homogenized by 10 strokes of a tight-fitted pestle in a dounce homogenizer. The lysate was incubated for 30 min on ice and spun for 10 min at 20,000g. The supernatant was subjected to an additional ultracentrifugation step for 1 h at 100,000g. The supernatant was recovered and rapidly frozen in liquid nitrogen or immediately processed further.

5.4.2 Lysate preparation for membrane proteins

About 1×10^9 adherent cells (average) were harvested with a cell scrapper and washed 3 times in ice-cold PBS (3 min, 550g). Collected cells were frozen in liquid nitrogen or immediately processed further. For cell lysis, the cell pellet was resuspended in 10 ml of Membrane-Lysis buffer (50 mM Tris, pH 7.4; 7.5 % Glycerol; 1 mM EDTA; 150 mM NaCl; 25 mM NaF; 1 mM Na₃VO₄; 1 mM DTT; containing 1 tablet of EDTA-free Protease inhibitor cocktail (Complete™, Roche) per 25 ml of buffer) and homogenized by 10 strokes of a tight-fitted pestle in a dounce homogenizer. The lysate was spun for 10 min at 750g, the supernatant was recovered and subjected to an ultracentrifugation step for 1 h at 100,000g. The membrane pellet was resuspended in 7,5 ml of Membrane-Lysis buffer containing 0.8% n-Dodecyl-β-D-maltoside and incubated for 1 h at 4°C with constant agitation. The sample was subjected to another ultracentrifugation step for 1h at 100,000g and the solubilized material was quickly frozen in liquid nitrogen or immediately processed further.

5.4.3 Lysate preparation for nuclear proteins

About 1×10^9 adherent cells (average) were harvested with a cell scrapper and washed 3 times in ice-cold PBS (3 min, 550g). Collected cells were frozen in liquid nitrogen or immediately processed further. For cell lysis, the cell pellet was resuspended in 10 ml of Hypotonic-Lysis buffer (10 mM Tris, pH 7.4; 1.5 mM MgCl₂; 10 mM KCl; 25 mM NaF; 1 mM Na₃VO₄; 1 mM DTT; containing 1 tablet of EDTA-free Protease inhibitor cocktail (Complete™, Roche) per 25 ml of buffer) and homogenized by 10 strokes of a tight-fitted pestle in a dounce homogenizer. The lysate was spun for 10 min at 2,000g and the resulting supernatant (S1) saved on ice. The nuclear pellet (P1) was resuspended in 5 ml Nuclear-Lysis buffer (50 mM Tris, pH 7.4; 1.5 mM MgCl₂; 20 % Glycerol; 420 mM NaCl; 25 mM NaF; 1 mM Na₃VO₄; 1 mM DTT; containing 1 tablet of EDTA-free Protease inhibitor cocktail (Complete™, Roche) per 25 ml of buffer) and incubated for 30 min on ice. The sample was combined with S1, further diluted with 7 ml of Dilution buffer (110 mM Tris, pH 7.4; 0.7 % NP40; 1.5 mM MgCl₂; 25 mM NaF; 1 mM Na₃VO₄; 1 mM DTT), incubated on ice for 10 min and centrifuged at 100,000g for 1h. The final supernatant (S2) was frozen quickly in liquid nitrogen.

5.4.4 Tandem Affinity Purification

The frozen lysate was quickly thawed in a 37°C water bath, and spun for 20 min at 100,000g. The supernatant was recovered and incubated with 0.2 ml of settled rabbit IgG-Agarose beads (Sigma) for 2 h with constant agitation at 4°C. Immobilized protein complexes were washed with 10 ml of CZ lysis buffer (containing 1 Complete™ tablet (Roche) per 50 ml of buffer) and further washed with 5 ml of TEV cleavage buffer (10 mM Tris, pH 7.4; 100 mM NaCl; 0.1 % IGEPAL; 0.5 mM EDTA; 1 mM DTT). Protein-complexes were eluted by incubation with 5 µl of TEV protease (GibcoBRL, Cat.No. 10127-017) for 1 h at 16°C in 150 µl TEV cleavage buffer. The eluate was recovered and combined with 0.2 ml settled Calmodulin affinity beads (Stratagene) in 0.2 ml CBP binding buffer (10 mM Tris, pH 7.4; 100 mM NaCl; 0.1 % IGEPAL; 2mM MgAc; 2mM Imidazole; 1mM DTT; 4 mM CaCl₂) followed by 1 h incubation at 4°C with constant agitation. Immobilized protein complexes were washed with 10 ml of CBP wash buffer (10 mM Tris, pH 7.4; 100 mM NaCl; 0.1 % IGEPAL; 1mM MgAc; 1mM Imidazole; 1mM DTT; 2 mM CaCl₂) and eluted by addition of 600 µl CBP elution buffer (10 mM Tris, pH

8.0; 5 mM EGTA) for 5 min at 37°C. The eluate was recovered in a siliconized tube and lyophilized. The remaining Calmodulin resin was boiled for 5 min in 50 µl 4x Laemmli sample buffer. The sample buffer was isolated, combined with the lyophilised fraction and loaded on a NuPAGE gradient gel (Invitrogen, 4-12%, 1.5 mm, 10 well).

5.4.5 Isolation of the Sambiasin complex of the invention from mouse tissue

Two mouse forebrains (0.6314 g total wet weight) were lysed in 14 mls of 50 mM HEPES pH 7.4; 150 mM NaCl; 1 mM EDTA; 0.5 mM Sodium Vanadate; 10% Glycerol; 1% n-Dodecyl-β-D-maltoside containing standard proteinase inhibitors. The tissue was homogenised in a Warring blender for 30 seconds on ice. Homogenates were incubated on ice for 1 hour and then centrifuged at 13,000 g for 30 min at 4°C. The resulting pellet was stored at -80°C while the supernatant was centrifuged at 50,000 g for 30 min at 4°C and the resulting pellet was also stored at -80°C. 6.5 ml of the supernatant from this second centrifugation step was taken and combined with 25 µl of anti presenilin-1 antisera (MAB5232, Chemicon). The antibody/lysate mixture was incubated for 1 hour at 4°C with end-over end mixing. Pre-washed protein G sepharose was added and the mixture was incubated overnight at 4°C with end-over mixing. The protein G was recovered by centrifugation at 200 g for 5 min at 4°C. The protein G beads were then washed 5 times in 1ml lysis buffer (containing 0.1% n-Dodecyl-β-D-maltoside rather than 1%). 100 µl of NuPAGE sample buffer (Invitrogen) was added and the sample incubated at 37°C for 10 min. Samples were separated on 4-12 % NuPAGE bis/tris gels (Invitrogen, 1.5 mm, 10 well). Proteins were visualized by staining with colloidal coomassie (Sigma) and then analysed by LC/MSMS.

5.5 Protein identification by mass spectrometry

5.5.1 Protein digestion prior to mass spectrometric analysis

Gel-separated proteins were reduced, alkylated and digested in gel essentially following the procedure described by Shevchenko et al., 1996, Anal. Chem. 68:850-858. Briefly, gel-separated proteins were excised from the gel using a clean scalpel, reduced

using 10 mM DTT (in 5mM ammonium bicarbonate, 54°C, 45 min) and subsequently alkylated with 55 mM iodoacetamid (in 5 mM ammonium bicarbonate) at room temperature in the dark (30 min). Reduced and alkylated proteins were digested in gel with porcine trypsin (Promega) at a protease concentration of 12.5 ng/μl in 5mM ammonium bicarbonate. Digestion was allowed to proceed for 4 hours at 37°C and the reaction was subsequently stopped using 5 μl 5% formic acid.

5.5.2 Sample preparation prior to analysis by mass spectrometry

Gel plugs were extracted twice with 20 μl 1% TFA and pooled with acidified digest supernatants. Samples were dried in a vacuum centrifuge and resuspended in 13 μl 1% TFA.

5.5.3 Mass spectrometric data acquisition

Peptide samples were injected into a nano LC system (CapLC, Waters or Ultimate, Dionex) which was directly coupled either to a quadrupole TOF (QTOF2, QTOF Ultima, QTOF Micro, Micromass or QSTAR Pulsar, Sciex) or ion trap (LCQ Deca XP) mass spectrometer. Peptides were separated on the LC system using a gradient of aqueous and organic solvents (see below). Solvent A was 5% acetonitrile in 0.5% formic acid and solvent B was 70% acetonitrile in 0.5% formic acid.

| Time (min) | % solvent A | % solvent B |
|------------|-------------|-------------|
| 0 | 95 | 5 |
| 5.33 | 92 | 8 |
| 35 | 50 | 50 |
| 36 | 20 | 80 |
| 40 | 20 | 80 |
| 41 | 95 | 5 |
| 50 | 95 | 5 |

Peptides eluting off the LC system were partially sequenced within the mass spectrometer.

5.5.4 Protein identification

The peptide mass and fragmentation data generated in the LC-MS/MS experiments were used to query fasta formatted protein and nucleotide sequence databases maintained and updated regularly at the NCBI (for the NCBInr, dbEST and the human and mouse genomes) and European Bioinformatics Institute (EBI, for the human, mouse, *D. melanogaster* and *C. elegans* proteome databases). Proteins were identified by correlating the measured peptide mass and fragmentation data with the same data computed from the entries in the database using the software tool Mascot (Matrix Science; Perkins et al., 1999, Electrophoresis 20:3551-3567). Search criteria varied depending on which mass spectrometer was used for the analysis.

TABLE 1

COMPONENTS OF COMPLEXES

| Name of complex | Entry Point | All interactors of the complex | Known interactors of the complex | Novel interactors of the complex | Proteins of unknown function |
|-----------------|-------------|--------------------------------|----------------------------------|----------------------------------|------------------------------|
| mDAB1-complex | mDAB1 | ACE | | ACE | |
| | | APG-1 | | APG-1 | |
| | | APLP1 | APLP1 | | |
| | | APLP2 | APLP2 | | |
| | | ApoE receptor 2 | ApoE receptor 2 | | |
| | | APP | APP | | |
| | | Archvillin | | Archvillin | |
| | | Contactin1 | | Contactin1 | |
| | | CRK | | CRK | |
| | | CRKL | | CRKL | |
| | | CSNK1D | | CSNK1D | |
| | | CSNK1E | | CSNK1E | |
| | | DAB1 | DAB1 | | |
| | | DAB2IP | | DAB2IP | |
| | | DNAJB1 | | DNAJB1 | DNAJB1 |

| | | | | |
|--|--|--|---|----------------------------------|
| | hypothetical protein FLJ11151 | | hypothetical protein FLJ11151 | hypothetical protein FLJ11151 |
| | Hypothetical protein FLJ31432 | | Hypothetical protein FLJ31432 | Hypothetical protein FLJ31432 |
| | <i>ISL1</i> | | <i>ISL1</i> | |
| | <i>ITGA1</i> | | <i>ITGA1</i> | |
| | <i>ITGB1</i> | | <i>ITGB1</i> | |
| | <i>LDLR</i> | | <i>LDLR</i> | |
| | <i>MAPK8IP3/JIP3</i> | | <i>MAPK8IP3/JIP3</i> | |
| | <i>NEDD5</i> | | <i>NEDD5</i> | |
| | <i>PLK</i> | | <i>PLK</i> | |
| | Proto-oncogene tyrosine kinase FYN (P59-FYN, SYN, SLK) isoform 1 | | Proto-oncogene tyrosine kinase FYN (P59-FYN, SYN, SLK) isoform 1 | |
| | <i>QPRT</i> | | <i>QPRT</i> | |
| | <i>S-100 beta</i> | | <i>S-100 beta</i> | |
| | <i>SIM TO PLEXIN 1 -</i> <i>MOUSE.</i> | | <i>SIM TO PLEXIN 1 -</i> <i>MOUSE.</i> | |
| | <i>TGM5</i> | | <i>TGM5</i> | |
| | <i>VLDL receptor</i> | | <i>VLDL receptor</i> | |

| | | | | |
|----------------|---|-------------------|---|--|
| JIP1-complex | JIP1 | ALPHA-CENTRACTIN. | | ALPHA-CENTRACTIN. |
| | APP | APP | | |
| | CASPASE-14 PRECURSOR. | | CASPASE-14 PRECURSOR. | |
| | DCTN1 | | DCTN1 | |
| | Dynactin 3, isoform 2 | | Dynactin 3, isoform 2 | |
| | HARP11, UNCHARACTERIZED HYPOTHALAMUS PROTEIN. | | HARP11, UNCHARACTERIZED HYPOTHALAMUS PROTEIN. | HARP11, UNCHARACTERIZE D HYPOTHALAMUS PROTEIN. |
| | ISLET-BRAIN 2. | | ISLET-BRAIN 2. | |
| | JIP-1 | JIP-1 | | |
| | JNK | JNK | | |
| | Kif5c | | | |
| | KINESIN HC | | | KINESIN HC |
| | KINESIN LC1. | | | KINESIN LC1. |
| | MAPK8IP3/JIP3 | | | MAPK8IP3/JIP3 |
| Fe65L2-complex | APLP1 | APLP1 | | |
| | | APLP2 | APLP2 | |

| | | | |
|--|--|--|--|
| | APP | APP | CDC42BPB |
| | CDC42BPB | | Contactin1 |
| | Contactin1 | | COP9 |
| | COP9 | COP9 COMPLEX SUBUNIT 4. | COP9 COMPLEX SUBUNIT 4. |
| | COP9 complex subunit 7a | COP9 complex subunit 7a | COP9 complex subunit 7a |
| | COPS3 | COPS3 | COPS3 |
| | COPS5 | COPS5 | COPS5 |
| | COPS6: COP9 subunit 6 (MOV34 homolog, 34 kD) | COPS6: COP9 subunit 6 (MOV34 homolog, 34 kD) | COPS6: COP9 subunit 6 (MOV34 homolog, 34 kD) |
| | COPS7B | COPS7B | COPS7B |
| | CUL3 | CUL3 | CUL3 |
| | Fe65L2 | Fe65L2 | FLJ12599 |
| | FLJ12599 | FLJ12599 | FLJ12599 |
| | GPR49 | GPR49 | GPR49 |
| | GPS1 | GPS1 | KIAA1102 PROTEIN (FRAGMENT). |
| | KIAA1102 PROTEIN (FRAGMENT). | KIAA1102 PROTEIN (FRAGMENT). | KIAA1102 PROTEIN (FRAGMENT). |
| | NEDD8 | NEDD8 | |

| | | | | |
|-------------------|-------------------------|----------------------------------|----------------------------------|----------------------------------|
| | Protocadherin gamma C3 | | Protocadherin gamma C3 | Protocadherin gamma C3 |
| | RBX1 | | RBX1 | |
| | RHOBTB1 | | RHOBTB1 | RHOBTB1 |
| | RHOBTB2 | | RHOBTB2 | RHOBTB2 |
| | SIM TO CGI-20 | | SIM TO CGI-20 | SIM TO CGI-20 |
| | SIMILAR TO POLYPROTEIN. | | SIMILAR TO POLYPROTEIN. | SIMILAR TO POLYPROTEIN. |
| | TRIP15 | | TRIP15 | |
| | TUBGCP3 | | TUBGCP3 | |
| | USP11 | | USP11 | USP11 |
| PilT/TJP4-complex | PilT/TJP4 | DLG1 | DLG1 | DLG1 |
| | | HYPOTHETICAL PROTEIN (FRAGMENT). | HYPOTHETICAL PROTEIN (FRAGMENT). | HYPOTHETICAL PROTEIN (FRAGMENT). |
| | | HYPOTHETICAL PROTEIN FLJ12599. | HYPOTHETICAL PROTEIN FLJ12599. | HYPOTHETICAL PROTEIN FLJ12599. |
| | | HYPOTHETICAL PROTEIN FLJ35393. | HYPOTHETICAL PROTEIN FLJ35393. | HYPOTHETICAL PROTEIN FLJ35393. |
| | | KIAA1102 (Fragment) | KIAA1102 (Fragment) | KIAA1102 |

| | | (Fragment) |
|--------------|-------------------------------|-------------------------------|
| | KIAA1949 (FRAGMENT) | KIAA1949 (FRAGMENT) |
| Pilt | Pilt | |
| STMN3 | STMN3 | |
| X11beta | X11beta | |
| Neurotrypsin | ADAMTS1 | ADAMTS1 |
| n-complex | ADAMTS19 | ADAMTS19 |
| | ADAMTS7 | ADAMTS7 |
| | CHRNA5 | CHRNA5 |
| | CRTAP | CRTAP |
| | CU70_HUMAN | CU70_HUMAN |
| | DEC R1 | DEC R1 |
| | DNAJC3 | DNAJC3 |
| | ERP70 | ERP70 |
| | GBT S1 | GBT S1 |
| | GRCB | GRCB |
| | hyou1: hypoxia up-regulated 1 | hyou1: hypoxia up-regulated 1 |

| | | | |
|--|--|--|--|
| | Hypothetical protein KIAA1402 (Fragment) | KIAA1402 (Fragment) (Fragment) | Hypothetical protein KIAA1402 (Fragment) (Fragment) |
| | LAMB1 | LAMB1 | |
| | Laminin, gamma 1 | Laminin, gamma 1 | |
| | MT-ACT48 | MT-ACT48 | MT-ACT48 |
| | Neurotrypsin | Neurotrypsin | |
| | NOTCH4-like protein (Hypothetical protein) | NOTCH4-like protein (Hypothetical protein) | |
| | PCDH16 | PCDH16 | PCDH16 |
| | PLOD | PLOD | |
| | PLOD3 | PLOD3 | |
| | PUTATIVE DNA POLYMERASE DELTA P38 SUBUNIT. | PUTATIVE DNA POLYMERASE DELTA P38 SUBUNIT. SUBUNIT. | PUTATIVE DNA POLYMERASE DELTA P38 SUBUNIT. SUBUNIT. |
| | q8wwi0 | q8wwi0 | q8wwi0 |
| | RAB39, MEMBER RAS ONCOGENE FAMILY. | RAB39, MEMBER RAS ONCOGENE FAMILY. | RAB39, MEMBER RAS ONCOGENE FAMILY. |
| | Reelin | Reelin | |

| | SC65 | SC65 | SC65 | SC65 |
|-----------------|--|----------------|--|--|
| | Similar to hydroxysteroid 17-beta dehydrogenase 11 | | Similar to hydroxysteroid 17-beta dehydrogenase 11 | Similar to hydroxysteroid 17-beta dehydrogenase 11 |
| | Similar to hypothetical protein FLJ22329 | | Similar to hypothetical protein FLJ22329 | Similar to hypothetical protein FLJ22329 |
| | Similar to RIKEN cDNA 1300010F03 gene | | Similar to RIKEN cDNA 1300010F03 gene | Similar to RIKEN cDNA 1300010F03 gene |
| | UGCGL2 | | UGCGL2 | UGCGL2 |
| Hunc18a-complex | Hunc18a | ELAVL1 | ELAVL1 | ELAVL1 |
| | Epim | Epim | Epim | Epim |
| | FIGF | FIGF | FIGF | FIGF |
| | Filamin, gamma | Filamin, gamma | Filamin, gamma | Filamin, gamma |
| | GOLGA3 | GOLGA3 | GOLGA3 | GOLGA3 |
| | Hunc18a | Hunc18a | Hunc18a | Hunc18a |
| | hypothetical protein BC013764 | | hypothetical protein BC013764 | hypothetical protein BC013764 |
| | PAWR | | PAWR | PAWR |

| | | | |
|-----------------------|---------------------------|---------------------------|---|
| | STX1A | STX1A | |
| | STX1B2 | STX1B2 | |
| | STX3A | STX3A | |
| | X11alpha | X11alpha | |
| | X11beta | X11beta | |
| Telencephalin-complex | APOD | APOD | |
| n | CALD1 | CALD1 | |
| | CALR | CALR | |
| | CD11a/CD18 | CD11a/CD18 INTEGRIN, | |
| | INTEGRIN, BETA-2 | BETA-2 | |
| | CHRNA5 | CHRNA5 | |
| | HYPOTHETICAL | HYPOTHETICAL | |
| | PROTEIN FLJ35393. | PROTEIN FLJ35393. | |
| | OPA1 | OPA1 | |
| | Presenilin 1 | Presenilin 1 | |
| | PYCS | PYCS | |
| | RAB6A | RAB6A | |
| | RAP1, GTP-GDP | RAP1, GTP-GDP | |
| | dissociation stimulator 1 | dissociation stimulator 1 | |
| | | | 1 |

| | | | | |
|--------------|----------------------|---------------------------------------|--|--|
| | | Telencephalin | Telencephalin | |
| PC7-complex | PC7 | 15 KDA SELENO-PROTEIN PRECURSOR. | | 15 KDA SELENO-PROTEIN PRECURSOR. |
| | APP-C99 | BACE1 | DNAJC3 | APP-C99 |
| | BACE1 | DNAJC3 | DNAJC3 | |
| | DNAJC3 | Neurotrypsin | | |
| | Neurotrypsin | | | |
| | PC7 | PC7 | Protocadherin beta 7 | Protocadherin beta 7 |
| | Protocadherin beta 7 | | | |
| VTRP-complex | VTRP | 27 KDA GOLGI SNARE PROTEIN. | PTPN1 | PTPN1 |
| | | ALPHA-SOLUBLE NSF ATTACHMENT PROTEIN. | 27 KDA GOLGI SNARE PROTEIN. | |
| | | | ALPHA-SOLUBLE NSF ATTACHMENT PROTEIN. | |
| | | | AMYLOID BETA A4 PRECURSOR PROTEIN-BINDING FAMILY B MEMBER 1. | AMYLOID BETA A4 PRECURSOR PROTEIN-BINDING FAMILY B MEMBER 1. |

| | | |
|--|---|---|
| | BCL2/ADENOVIRUS E1B 19KD- INTERACTING PROTEIN 1, ISOFORM BNIP1. | BCL2/ADENOVIRUS E1B 19KD- INTERACTING PROTEIN 1, ISOFORM BNIP1. |
| | BET1 | BET1 |
| | CALPAIN SMALL SUBUNIT. | CALPAIN SMALL SUBUNIT. |
| | CENTROMERE/KINETO CHORE PROTEIN ZW10 HOMOLOG. | CENTROMERE/KINET OCHORE PROTEIN ZW10 HOMOLOG. |
| | DYNACTIN COMPLEX 50 KDA SUBUNIT. | DYNACTIN COMPLEX 50 KDA SUBUNIT. |
| | GP25L2 PROTEIN. | GP25L2 PROTEIN. |
| | HSPC009. | HSPC009. |
| | HYPOTH 61.5 KDA PROTEIN (FRAGMENT). | HYPOTH 61.5 KDA PROTEIN (FRAGMENT). |
| | HYPOTH 78.2 KDA PROTEIN (FRAGMENT). | HYPOTH 78.2 KDA PROTEIN (FRAGMENT). |

| | | |
|--|--|---|
| MDS032, UNCHARACTERIZED HEMATOPOIETIC STEM/PROGENITOR CELLS PROTEIN. | MDS032, UNCHARACTERIZED HEMATOPOIETIC STEM/PROGENITOR CELLS PROTEIN. | MDS032, D HEMATOPOIETIC STEM/PROGENITOR CELLS PROTEIN. |
| NEUROBLASTOMA- AMPLIFIED PROTEIN. | | NEUROBLASTOMA- AMPLIFIED PROTEIN. |
| Phosphatidylserine receptor | Phosphatidylserine receptor | Phosphatidylserine receptor |
| RAD50-INTERACTING PROTEIN 1. | RAD50-INTERACTING PROTEIN 1. | RAD50-INTERACTING PROTEIN 1. |
| SEC22B VESICLE TRAFFICKING PROTEIN | SEC22B VESICLE TRAFFICKING PROTEIN | SEC22B VESICLE TRAFFICKING PROTEIN |
| Similar to golgi SNAP receptor complex member 1 | | Similar to golgi SNAP receptor complex member 1 |
| SYNTAXIN 10. | | SYNTAXIN 10. |
| SYNTAXIN 18. | | SYNTAXIN 18. |
| SYNTAXIN 5. | | SYNTAXIN 5. |

| | VESICULAR-FUSION PROTEIN NSF. | VESICULAR-FUSION PROTEIN NSF. |
|----------------------------|---|---|
| | VTRP | VTRP |
| BACE1 (new)- complex | BACE1 BACE1 (new) | BACE1 |
| | Cadherin EGF LAG seven-pass G-type receptor 2 | Cadherin EGF LAG seven-pass G-type receptor 2 |
| | Calsyntenin 1 | Calsyntenin 1 |
| | CGI-13 | CGI-13 |
| | Delta-6 fatty acid desaturase | Delta-6 fatty acid desaturase |
| | Delta-like homolog | Delta-like homolog |
| | FLJ30668 | FLJ30668 |
| | FLJ39249 | FLJ39249 |
| | integral membrane transporter protein | integral membrane transporter protein |
| | ITCH | ITCH |
| | KIAA1250 | KIAA1250 |
| | Kinecin 1 (kinesin receptor) | Kinecin 1 (kinesin receptor) |

| | | | |
|---------------|---------------------------------------|---------------------------------------|---------------------------------------|
| Nicastrin | Nicastrin | | |
| Nogo-A | | Nogo-A | |
| PDGFRB | | PDGFRB | |
| PTK7 | | PTK7 | |
| SERPINA1 | | SERPINA1 | |
| | SIM TO Y71H10A. 2.P. | SIM TO Y71H10A. 2.P. | SIM TO Y71H10A. |
| | | | 2.P. |
| | Sortilin-related receptor | Sortilin-related receptor | |
| | | STX10 | |
| | Thioredoxin domain-containing protein | Thioredoxin domain-containing protein | Thioredoxin domain-containing protein |
| BACE2 | APLP2 | APLP2 | |
| BACE2-complex | BACE2 | BACE2 | Cadherin EGF LAG |
| | | | seven-pass G-type |
| | | | receptor 2 |
| | | | Calsyntenin 1 |
| | | | Delta-like homolog |
| | | | FLJ10474 |
| | | | FLJ14787 |
| | | | FLJ14787 |

| | | | | |
|--------------------------|--|---------|--|--|
| | Integral membrane transporter protein | | Integral membrane transporter protein | |
| | ITCH | | ITCH | |
| | KIAA1949 (FRAGMENT) | | KIAA1949 (FRAGMENT) | KIAA1949 (FRAGMENT) |
| | STX10 | | STX10 | |
| PALADIN- PALADIN complex | AOP2 | | AOP2 | |
| | fij11198, member of the abc transporter family | | fij11198, member of the abc transporter family | fij11198, member of the abc transporter family |
| | Paladin | Paladin | | |
| | Similar to BCL2-associated athanogene 2 (Hypothetical protein) | | Similar to BCL2-associated athanogene 2 (Hypothetical protein) | Similar to BCL2-associated athanogene 2 (Hypothetical protein) |
| | TNRC6 | | TNRC6 | TNRC6 |
| | USP7 | | USP7 | |
| TFCP2- TFCP2 complex | Fe65 | Fe65 | | LBP-9 |
| | LBP-9 | | | RR42_HUMAN |
| | RR42_HUMAN | | | RR42_HUMAN |

| | | | |
|-----------------|---|---|---|
| | TF LBP-1b | | TF LBP-1b |
| | TFCP2 | TFCP2 | |
| | TRAP25 | TRAP25 | |
| p75 NTR-complex | Cadherin EGF LAG seven-pass G-type receptor 2 | Cadherin EGF LAG seven-pass G-type receptor 2 | |
| | DKFZP586F1524 protein | DKFZP586F1524 protein | DKFZP586F1524 protein |
| | HYPOTHETICAL PROTEIN FLJ39249 | HYPOTHETICAL PROTEIN FLJ39249 | HYPOTHETICAL PROTEIN FLJ39249 |
| | Nogo receptor | Nogo receptor | Nogo receptor |
| | NRAGE/MAGED1 | NRAGE/MAGED1 | NRAGE/MAGED1 |
| | p75 NTR | p75 NTR | p75 NTR |
| | Rho-GDI | Rho-GDI | Rho-GDI |
| | Thioredoxin domain-containing protein | Thioredoxin domain-containing protein | Thioredoxin domain-containing protein |
| | VAPA | VAPA | VAPA |
| Lamezin-complex | ASPH | ASPH | ASPH |
| | bzw1: basic leucine zipper and w2 domains 1 | bzw1: basic leucine zipper and w2 domains 1 | bzw1: basic leucine zipper and w2 domains 1 |

| | | | 1 | domains 1 |
|--|--|--|--|---------------|
| | C7orf14 | | C7orf14 | |
| | CLNS1A | | CLNS1A | |
| | CLU: clusterin (complement lysis inhibitor, SP-40,40, sulfated glycoprotein 2, testosterone-repressed prostate message 2, apolipoprotein J) | | CLU: clusterin (complement lysis inhibitor, SP-40,40, sulfated glycoprotein 2, testosterone-repressed prostate message 2, apolipoprotein J) | |
| | CNTNAP1 | | CNTNAP1 | |
| | COX5B | | COX5B | |
| | COX6B | | COX6B | |
| | COX6C | | COX6C | |
| | CSGlcA-T | | CSGlcA-T | CSGlcA-T |
| | DICER1 | | DICER1 | |
| | dkfzp586c1924 | | dkfzp586c1924 | dkfzp586c1924 |
| | DREV1 | | DREV1 | DREV1 |
| | EC 6.3.2.19 (Fragment) | | EC 6.3.2.19 (Fragment) | |
| | EIF2B2 | | EIF2B2 | |

| | | | | | | | | | | |
|--|---|--|--|-----------------|---|--|--|--|--|--|
| | | | | ensp00000258417 | | | | ensp00000258417 | | ensp00000258417 |
| | EXTL2 | | | | EXTL2 | | | EXTL2 | | EXTL2 |
| | G2AN | | | | G2AN | | | | | |
| | Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase | | | | Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase | | | | | |
| | 3 | | | | e 3 | | | | | |
| | HIV-1 Vpr-binding protein (Fragment) | | | | HIV-1 Vpr-binding protein (Fragment) | | | HIV-1 Vpr-binding protein (Fragment) | | HIV-1 Vpr-binding protein (Fragment) |
| | HPIP | | | | HPIP | | | HPIP | | HPIP |
| | HSPC329 (Fragment) | | | | HSPC329 (Fragment) | | | HSPC329 (Fragment) | | HSPC329 (Fragment) |
| | hyou1: hypoxia up-regulated 1 | | | | hyou1: hypoxia up-regulated 1 | | | hyou1: hypoxia up-regulated 1 | | hyou1: hypoxia up-regulated 1 |
| | Hypothetical protein FLJ34763 | | | | Hypothetical protein FLJ34763 | | | Hypothetical protein FLJ34763 | | Hypothetical protein FLJ34763 |
| | Hypothetical protein KIAA0062 (Fragment) | | | | Hypothetical protein KIAA0062 (Fragment) | | | Hypothetical protein KIAA0062 (Fragment) | | Hypothetical protein KIAA0062 (Fragment) |
| | Hypothetical protein KIAA1500 (Fragment) | | | | Hypothetical protein KIAA1500 (Fragment) | | | Hypothetical protein KIAA1500 (Fragment) | | Hypothetical protein KIAA1500 (Fragment) |

| | | | |
|--|--------------|--|--|
| HYPOTHETICAL PROTEIN KIAA1524 (FRAGMENT). | | HYPOTHETICAL PROTEIN KIAA1524 (FRAGMENT). | HYPOTHETICAL PROTEIN KIAA1524 (FRAGMENT). |
| HYPOTHETICAL PROTEIN. | | HYPOTHETICAL PROTEIN. | HYPOTHETICAL PROTEIN. |
| HYPOTHETICAL PROTEIN. | | HYPOTHETICAL PROTEIN. | HYPOTHETICAL PROTEIN. |
| IGF2R | | IGF2R | |
| ITGAV | | ITGAV | |
| ITPR2 | | ITPR2 | |
| KIAA1250, homolog of rat kinase D-interacting substance of 220 kDa | | KIAA1250, homolog of rat kinase D-interacting substance of 220 kDa | KIAA1250, homolog of rat kinase D-interacting substance of 220 kDa |
| Lamezin/FKRP | Lamezin/FKRP | | |
| Laminin, gamma 1 | | Laminin, gamma 1 | |
| LPHH1 | | LPHH1 | |
| MAGEB4 | | MAGEB4 | MAGEB4 |
| MGC5442 | | MGC5442 | MGC5442 |
| Neural cell adhesion molecule L1 | | Neural cell adhesion molecule L1 | |

| | | | |
|-------------|--|--|--|
| | Neurotrypsin | | Neurotrypsin |
| | Nuclear protein SDK3 | | Nuclear protein SDK3 |
| PPIB | | PPIB | |
| Presenilin1 | Presenilin1 | PTDSS1 | |
| PTDSS1 | | Reelin | |
| Reelin | | SCG2 | |
| SCG2 | SIMILAR TO HYPOTHETICAL PROTEIN SB153. | SIMILAR TO HYPOTHETICAL PROTEIN SB153. | SIMILAR TO HYPOTHETICAL PROTEIN SB153. |
| | Similar to RIKEN cDNA 1100001L14 gene (Fragment) | Similar to RIKEN cDNA 1100001L14 gene (Fragment) | Similar to RIKEN cDNA 1100001L14 gene (Fragment) |
| | | | |
| | | STR A6 isoform 1 | STR A6 isoform 1 |
| | | TLOC1 | |
| | | UGCGL2 | |
| | VESICULAR INTEGRAL-MEMBRANE PROTEIN VIP36 PRECURSOR | VESICULAR INTEGRAL- MEMBRANE PROTEIN VIP36 PRECURSOR | VESICULAR INTEGRAL- MEMBRANE PROTEIN VIP36 PRECURSOR |

| | | | | |
|------------|--------------------|----------|----------------------|------------|
| APP-C59- | APP-C59 | Wolfamin | | Wolfamin |
| complex | C59 | C59 | | |
| | Copine III | | Copine III | Copine III |
| | COPS3 | | COPS3 | |
| | CPNE7 | | CPNE7 | CPNE7 |
| | CUL3 | | CUL3 | |
| | Fee65 | Fee65 | | |
| | Fee65L1 | Fee65L1 | | |
| | GTF3C3 | | GTF3C3 | |
| | NRD1 | | NRD1 | |
| | S100 beta | | S100 beta | |
| | TIP60 | TIP60 | | |
| | USP11 | | USP11 | |
| | X11beta | X11beta | | |
| BRI/ITM2B- | BRI/ITM2B | APLP2 | APLP2 | |
| complex | | | | |
| | APP | | APP | |
| | CARBOXYPEPTIDASE D | | CARBOXYPEPTIDASE E D | |
| | Contactin1 | | Contactin1 | |

| Delta-like homolog | Delta-like homolog | Delta-like homolog | Delta-like homolog |
|---|---|---|---|
| DPP6 (DIPEPTIDYL AMINOPEPTIDASE-LIKE PROTEIN 6) |
| Integral membrane protein 2B (ITM2B) | Integral membrane protein | | |
| ITM2C | ITM2C | ITM2C | ITM2C |

TABLE 2

INDIVIDUAL PROTEINS OF THE COMPLEXES

| Protein name | | SEQ ID | IPI number | Molecular weight |
|--|-----|---------------|------------|------------------|
| APP | 5 | IPI00006608.1 | 86943 | |
| 15 KDA SELENO- PROTEIN PRECURSOR. | 127 | IPI00030877.1 | 17743 | |
| 27 KDA GOLGI SNARE PROTEIN. | 133 | IPI00023135.1 | 24775 | |
| ACE | 1 | IPI00025852.1 | 149715 | |
| ADAMTS1 | 75 | IPI00005908.1 | 105384 | |
| ADAMTS19 | 76 | IPI00152639.1 | 134062 | |
| ADAMTS7 | 77 | IPI00007692.1 | 109695 | |
| ALPHA-CENTRACTIN. | 31 | IPI00029468.1 | 42614 | |
| ALPHA-SOLUBLE NSF ATTACHMENT PROTEIN. | 134 | IPI00009253.1 | 33247 | |
| AMYLOID BETA A4 PRECURSOR PROTEIN-BINDING FAMILY B MEMBER 1. | 135 | IPI00010843.1 | 77244 | |
| AOP2 | 178 | IPI00024912.1 | 24904 | |
| APG-1 | 2 | IPI00032918.1 | 94505 | |
| APLP1 | 3 | IPI00020012.2 | 72176 | |
| APLP1 | 42 | IPI00020012.1 | 72176 | |
| APLP2 | 4 | IPI00031030.1 | 86956 | |
| APOD | 117 | IPI00006662.1 | 21276 | |

| | | | |
|--|-----|---------------|----------|
| ApoE receptor 2 | 6 | IPI00005774.1 | 105716 |
| APP | 5 | IPI00006608.1 | 86943 |
| APP-C99 | 128 | CZB0000004.1 | 11277.92 |
| Arch villin | 7 | IPI00170232.1 | 243162 |
| ASPH | 194 | IPI00029224.1 | 85498 |
| BACE1 | 129 | IPI00011518.1 | 55764 |
| BACE2 | 175 | IPI00001954.1 | 56180 |
| BCL2/ADENOVIRUS E1B 19KD-INTERACTING PROTEIN 1, ISOFORM BNIP1. | 136 | IPI00014022.1 | 26217 |
| BET1 | 137 | IPI00025163.1 | 13289 |
| bzw1: basic leucine zipper and w2 domains 1 | 236 | IPI00005681.1 | 48043 |
| C59 | 239 | CZB00000003.1 | 6834.89 |
| C7orf14 | 195 | IPI00022495.1 | 228049 |
| Cadherin EGF LAG seven-pass G-type receptor 2 | 157 | IPI00015346.1 | 317453 |
| CALD1 | 118 | IPI00011878.1 | 64256 |
| CALPAIN SMALL SUBUNIT. | 138 | IPI00025084.1 | 28316 |
| CALR | 119 | IPI00020599.1 | 48142 |
| Calsyntenin 1 | 158 | IPI00007257.1 | 109793 |
| CARBOXYPEPTIDASE D | 246 | IPI00027078.2 | 152915 |
| CASPASE-14 PRECURSOR. | 32 | IPI00013885.1 | 27680 |
| CD11a/CD18 INTEGRIN, BETA-2 | 120 | IPI00007039.1 | 84791 |
| CDC42BPB | 43 | IPI00005689.2 | 199210 |

| | | | |
|---|-----|---------------|--------|
| CENTROMERE/KINETOCHORE PROTEIN ZW10 HOMOLOG. | 139 | IPI00011631.1 | 88829 |
| CGI-13 | 156 | IPI00008847.1 | 52917 |
| CHRNA5 | 78 | IPI00105403.1 | 53311 |
| CLNS1A | 196 | IPI00004795.1 | 26215 |
| CLU: clusterin (complement lysis inhibitor, SP-40,40, sulfated glycoprotein 2, testosterone-repressed prostate message 2, apolipoprotein J) | 197 | IPI00219642.1 | 55192 |
| CNTNAP1 | 198 | IPI00219249.1 | 164756 |
| Contactin1 | 12 | IPI00029751.1 | 113320 |
| COP9 | 44 | IPI00009480.1 | 23226 |
| COP9 COMPLEX SUBUNIT 4 | 45 | IPI00163757.1 | 46378 |
| COP9 complex subunit 7a | 46 | IPI00033154.1 | 30277 |
| Copine III | 241 | IPI00024403.1 | 60131 |
| COPS3 | 47 | IPI00025721.1 | 47873 |
| COPS5 | 48 | IPI00009958.3 | 37452 |
| COPS6: COP9 subunit 6 (MOV34 homolog, 34 kD) | 49 | IPI00163230.1 | 33576 |
| COPS7B | 50 | IPI00009301.1 | 29622 |
| COX5B | 199 | IPI00021785.2 | 13696 |
| COX6B | 200 | IPI00216085.1 | 10192 |
| COX6C | 201 | IPI00015972.1 | 8781 |
| CPNE7 | 240 | IPI00002657.1 | 70294 |

| | | | |
|---|-----|---------------|--------|
| CRK | 8 | IPI00004838.1 | 33872 |
| CRKL | 9 | IPI00004839.1 | 33777 |
| CRTAP | 79 | IPI00007384.1 | 46562 |
| CSGlcA-T | 86 | IPI00018606.1 | 87640 |
| CSNK1D | 10 | IPI00011102.1 | 47330 |
| CSNK1E | 11 | IPI00027729.1 | 47315 |
| CU70_HUMAN | 80 | IPI00027898.3 | 25456 |
| CUL3 | 51 | IPI00014312.1 | 88930 |
| DAB1 | 13 | IPI00026889.2 | 59979 |
| DAB2IP | 14 | IPI00045600.1 | 117651 |
| DCTN1 | 33 | IPI00011446.1 | 127404 |
| DECR1 | 81 | IPI00003482.1 | 36068 |
| Delta-6 fatty acid desaturase | 159 | IPI00003544.1 | 52259 |
| Delta-like homolog | 160 | IPI00009191.1 | 41143 |
| DICER1 | 202 | IPI00012680.1 | 217628 |
| dkfzp586c1924 | 237 | IPI00031064.1 | 21527 |
| DKFZP586F1524 protein | 95 | IPI00165506.1 | 42031 |
| DLG1 | 67 | IPI00002554.1 | 103221 |
| DNAJB1 | 15 | IPI00015947.1 | 38044 |
| DNAJC3 | 82 | IPI00006713.1 | 57580 |
| DPP6 (DIPEPTIDYL AMINOPEPTIDASE-LIKE PROTEIN 6) | 247 | IPI00000823.1 | 97588 |

| | | | | |
|--|--|-----|---------------|--------|
| DREV1 | | 203 | IPI00100239.1 | 36536 |
| Dynactin 3, isoform 2 | | 34 | IPI00013654.1 | 19469 |
| DYNACTIN COMPLEX 50 KDA SUBUNIT. | | 140 | IPI00013802.1 | 44231 |
| EC 6.3.2.19 (Fragment) | | 204 | IPI00028307.1 | 143477 |
| EIF2B2 | | 205 | IPI00028083.1 | 38990 |
| ELAVL1 | | 105 | IPI00019360.2 | 36092 |
| ensp0000258417 | | 238 | IPI00216484.1 | 75579 |
| Epim | | 106 | IPI00031034.1 | 33312 |
| ERP70 | | 83 | IPI00009904.1 | 72932 |
| EXTL2 | | 206 | IPI00002732.1 | 37466 |
| Fe65 | | 135 | IPI00010843.1 | 77244 |
| Fe65L1 | | 242 | IPI00023841.1 | 81080 |
| Fe65L2 | | 53 | IPI00032785.1 | 52638 |
| FIGF | | 107 | IPI00004653.1 | 40444 |
| Filamin, gamma | | 108 | IPI00165017.1 | 291151 |
| FLJ10474 | | 176 | IPI00163721.1 | 199210 |
| flj11198, member of the abc transporter family | | 183 | IPI00019973.2 | 79745 |
| FLJ12599 | | 52 | IPI00182757.1 | 102917 |
| FLJ14787 | | 177 | IPI00102685.1 | 35274 |
| FLJ30668 | | 161 | IPI00043733.1 | 33338 |
| FLJ39249 | | 162 | IPI00167501.1 | 27459 |
| G2AN | | 207 | IPI00011454.1 | 109438 |

| | | | |
|---|-----|----------------|--------|
| Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3 | 208 | IPI00014931.1 | 37062 |
| GBT51 | 84 | IPI00002919.2 | 22329 |
| GOLGA3 | 109 | IPI001588673.1 | 170268 |
| GP25L2 PROTEIN. | 141 | IPI00030888.1 | 25122 |
| GPR49 | 54 | IPI00021131.1 | 99998 |
| GPS1 | 55 | IPI00156282.1 | 56481 |
| GRCB | 85 | IPI00003407.1 | 62265 |
| GTF3C3 | 243 | IPI00015806.1 | 101272 |
| HARP11, UNCHARACTERIZED HYPOTHALAMUS PROTEIN. | 35 | IPI00016170.2 | 47060 |
| HIV-1 Vpr-binding protein (Fragment) | 209 | IPI00155567.1 | 169450 |
| HPIP | 210 | IPI00100773.1 | 80643 |
| HSPC009. | 142 | IPI00022277.1 | 11731 |
| HSPC329 (Fragment) | 211 | IPI00000205.1 | 18247 |
| Hunc18a | 110 | IPI00046057.1 | 68736 |
| hyou1: hypoxia up-regulated 1 | 103 | IPI00000877.1 | 111335 |
| HYPOTH 61.5 KDa PROTEIN (FRAGMENT). | 143 | IPI00107712.1 | 61548 |
| HYPOTH 78.2 KDa PROTEIN (FRAGMENT). | 144 | IPI00141564.1 | 78194 |
| HYPOTHETICAL PROTEIN (FRAGMENT). | 68 | IPI00166518.1 | 112183 |
| hypothetical protein BC013764 | 116 | IPI00060715.1 | 35701 |
| hypothetical protein FLJ11151 | 30 | IPI00019937.1 | 35622 |
| HYPOTHETICAL PROTEIN FLJ12599. | 52 | IPI00182757.1 | 102917 |

| | | | | |
|---|--|-----|---------------|--------|
| Hypothetical protein FLJ31432 | | 16 | IPI00102281.1 | 36961 |
| Hypothetical protein FLJ34763 | | 215 | IPI00168126.1 | 50520 |
| HYPOTHETICAL PROTEIN FLJ35393. | | 69 | IPI00167994.1 | 21530 |
| HYPOTHETICAL PROTEIN FLJ39249 | | 162 | IPI00167501.1 | 27459 |
| Hypothetical protein KIAA0062 (Fragment) | | 216 | IPI00014236.1 | 58417 |
| Hypothetical protein KIAA1402 (Fragment) | | 86 | IPI00018606.1 | 87640 |
| Hypothetical protein KIAA1500 (Fragment) | | 217 | IPI00151706.2 | 126320 |
| HYPOTHETICAL PROTEIN KIAA1524 (FRAGMENT). | | 214 | IPI00001627.1 | 99841 |
| HYPOTHETICAL PROTEIN. | | 212 | IPI00028427.1 | 44941 |
| HYPOTHETICAL PROTEIN. | | 213 | IPI00015506.1 | 15066 |
| IGF2R | | 218 | IPI00007226.1 | 274309 |
| Integral membrane protein 2B (ITM2B) | | 249 | IPI00031821.1 | 30338 |
| Integral membrane transporter protein | | 173 | IPI00020093.1 | 31735 |
| ISL1 | | 17 | IPI00025071.1 | 39036 |
| ISLET-BRAIN 2. | | 36 | IPI00009277.1 | 84711 |
| ITCH | | 163 | IPI00061780.1 | 102803 |
| ITGA1 | | 18 | IPI00008244.1 | 127838 |
| ITGAV | | 219 | IPI00027505.1 | 116052 |
| ITGB1 | | 19 | IPI00009465.1 | 88465 |
| ITM2C | | 248 | IPI00185968.1 | 33329 |
| ITPR2 | | 220 | IPI00031545.1 | 308078 |

| | | | |
|--|-----|---------------|--------|
| JIP-1 | 37 | IPI00023133.1 | 77524 |
| JNK | 38 | IPI00129682.1 | 44229 |
| KIAA1102 (Fragment) | 70 | IPI00160387.1 | 121739 |
| KIAA1102 PROTEIN (FRAGMENT). | 56 | IPI00167860.1 | 123943 |
| KIAA1250, homolog of rat kinase D-interacting substance of 220 kDa | 164 | IPI00033429.1 | 197211 |
| KIAA1949 (FRAGMENT) | 71 | IPI00152853.1 | 73064 |
| Kif5c | 41 | IPI00028561.1 | 109495 |
| Kinetin 1 (kinesin receptor) | 174 | IPI00032968.1 | 156093 |
| KINESIN HC | 39 | IPI00012837.1 | 109685 |
| KINESIN LC1. | 40 | IPI00020096.1 | 64786 |
| LAMB1 | 87 | IPI00013976.1 | 198066 |
| Lamezin/FKRP | 222 | IPI00013281.1 | 54568 |
| Laminin, gamma 1 | 88 | IPI00003398.1 | 177607 |
| LBP-9 | 184 | IPI00005099.1 | 54627 |
| LDLR | 20 | IPI00000070.1 | 95376 |
| LPHH1 | 221 | IPI00017562.1 | 157178 |
| MAGEB4 | 223 | IPI00006737.1 | 38923 |
| MAPK8IP3/JIP3 | 21 | IPI00045524.1 | 147789 |
| MDS032, UNCHARACTERIZED HEMATOPOIETIC STEM/PROGENITOR CELLS | 145 | IPI00020515.1 | 29345 |
| PROTEIN. | | | |
| MGC5442 | 224 | IPI00027773.1 | 26261 |

| | | | |
|--|-----|---------------|--------|
| MT-ACT48 | 89 | IPI00032410.1 | 46355 |
| NEDD5 | 22 | IPI00014177.1 | 41487 |
| NEDD8 | 57 | IPI00020008.1 | 9072 |
| Neural cell adhesion molecule L1 | 225 | IPI00027087.1 | 140003 |
| NEUROBLASTOMA-AMPLIFIED PROTEIN. | 146 | IPI00026324.1 | 152546 |
| Neurotrypsin | 91 | IPI00011063.1 | 97012 |
| Nicastrin | 165 | IPI00021983.1 | 78411 |
| Nogo receptor | 190 | IPI00220122.1 | 54053 |
| Nogo-A | 166 | IPI00021766.3 | 129931 |
| NOTCH4-like protein (Hypothetical protein) | 90 | IPI00007830.1 | 29618 |
| NRAGE/MAGED1 | 189 | IPI00001829.2 | 86151 |
| NRD1 | 244 | IPI00014521.1 | 130945 |
| Nuclear protein Sdk3 | 226 | IPI00099225.1 | 81584 |
| OPA1 | 121 | IPI00107749.1 | 111822 |
| p75 NTR | 193 | IPI00027436.1 | 45183 |
| Paladin | 179 | IPI00161782.1 | 96754 |
| PWR | 111 | IPI00001871.1 | 36766 |
| PC7 | 130 | IPI00002882.1 | 86247 |
| PCDH16 | 92 | IPI00064262.1 | 346181 |
| PDGFRB | 167 | IPI00015902.1 | 123968 |
| Phosphatidylserine receptor | 147 | IPI00027294.1 | 47939 |
| Pilt | 72 | IPI00010544.2 | 60705 |

| | | | |
|--|-----|---------------|--------|
| PLK | 23 | IPI00021248.1 | 68255 |
| PLOD | 93 | IPI00027192.1 | 83580 |
| PLOD3 | 94 | IPI00030255.1 | 84785 |
| PPIB | 227 | IPI00107117.1 | 23743 |
| Presenilin1 | 123 | IPI00026333.1 | 52163 |
| Protocadherin beta 7 | 132 | IPI00001425.1 | 86707 |
| Protocadherin gamma C3 | 58 | IPI00001872.3 | 101077 |
| Proto-oncogene tyrosine kinase FYN (P59-FYN, SYN, SLK) isoform 1 | 24 | IPI00031350.1 | 63754 |
| PTDSS1 | 228 | IPI00010746.1 | 55528 |
| PTK7 | 168 | IPI00012719.1 | 118260 |
| PTPN1 | 131 | IPI00216465.1 | 54452 |
| PUTATIVE DNA POLYMERASE DELTA P38 SUBUNIT. | 95 | IPI00165506.1 | 42031 |
| PYCS | 122 | IPI00008982.1 | 87302 |
| q8wwi0 | 104 | IPI00103133.1 | 13878 |
| QPRT | 25 | IPI00015791.2 | 30816 |
| RAB39, MEMBER RAS ONCOGENE FAMILY. | 96 | IPI00167108.1 | 25007 |
| RAB6A | 124 | IPI00023526.1 | 23593 |
| RAD50-INTERACTING PROTEIN 1. | 148 | IPI00072244.1 | 93442 |
| RAP1, GTP-GDP dissociation stimulator 1 | 125 | IPI00107875.1 | 66331 |
| RBX1 | 59 | IPI00003386.1 | 12274 |
| Reelin | 97 | IPI00021018.1 | 388402 |

| | | | | |
|--|--|-----|---------------|--------|
| RHOBTB1 | | 60 | IPI00001317.1 | 79417 |
| RHOBTB2 | | 61 | IPI00008545.2 | 85137 |
| Rho-GDI | | 191 | IPI00003815.1 | 23207 |
| RR42_HUMAN | | 185 | IPI00014198.2 | 31835 |
| S-100 beta | | 26 | IPI00220413.1 | 10713 |
| SC65 | | 98 | IPI00023337.1 | 50381 |
| SCG2 | | 229 | IPI00009362.1 | 70869 |
| SEC22B VESICLE TRAFFICKING PROTEIN | | 149 | IPI00006865.1 | 24741 |
| SERPINA1 | | 169 | IPI00032180.1 | 46737 |
| SIM TO CGI-20 | | 62 | IPI00144290.1 | 36504 |
| SIM TO PLEXIN 1 - MOUSE. | | 27 | IPI00164586.1 | 208223 |
| SIM TO Y71H10A. 2.P. | | 170 | IPI00170775.1 | 68184 |
| Similar to BCL2-associated athanogene 2 (Hypothetical protein) | | 180 | IPI00130304.1 | 23474 |
| Similar to golgi SNAP receptor complex member 1 | | 153 | IPI00044920.1 | 20068 |
| Similar to hydroxysteroid 17-beta dehydrogenase 11 | | 100 | IPI00122464.1 | 33518 |
| Similar to hypothetical protein FLJ22329 | | 101 | IPI00002905.1 | 28319 |
| SIMILAR TO HYPOTHETICAL PROTEIN SB153. | | 230 | IPI00084084.3 | 86438 |
| SIMILAR TO POL POLYPROTEIN. | | 63 | IPI00093098.2 | 155047 |
| Similar to RIKEN cDNA 110001L14 gene (Fragment) | | 232 | IPI00062859.1 | 40583 |

| | | | |
|---------------------------------------|-----|---------------|--------|
| Similar to RIKEN cDNA 1300010F03 gene | 99 | IPI00122560.1 | 116226 |
| Sortilin-related receptor | 171 | IPI00022608.1 | 248441 |
| STMN3 | 73 | IPI00021199.2 | 21017 |
| STRA6 isoform 1 | 231 | IPI00154566.1 | 73533 |
| STX10 | 150 | IPI00012264.2 | 28114 |
| STX1A | 112 | IPI00003370.1 | 33023 |
| STX1B2 | 113 | IPI00065786.1 | 33245 |
| STX3A | 114 | IPI00012421.1 | 33141 |
| SYNTAXIN 10. | 150 | IPI00012264.2 | 28114 |
| SYNTAXIN 18. | 151 | IPI00027194.1 | 38674 |
| SYNTAXIN 5. | 152 | IPI00012005.1 | 34086 |
| Telencephalin | 126 | IPI00019003.2 | 97331 |
| TF LBP-1b | 186 | IPI00005018.1 | 60491 |
| TFCP2 | 187 | IPI00029650.1 | 57313 |
| TGM5 | 28 | IPI00003518.1 | 71919 |
| Thioredoxin domain-containing protein | 172 | IPI00001028.1 | 32535 |
| TIP60 | 245 | IPI00024400.1 | 58681 |
| TLOC1 | 233 | IPI00019004.1 | 45862 |
| TNRC6 | 181 | IPI00158479.1 | 210272 |
| TRAP25 | 188 | IPI00063213.1 | 20277 |
| TRIP15 | 64 | IPI00018813.1 | 51597 |
| TUBGCP3 | 65 | IPI00033516.1 | 103571 |

| | | | |
|---|-----|---------------|--------|
| UGCGL2 | 102 | IPI00024467.1 | 174761 |
| USP11 | 66 | IPI00184533.1 | 109817 |
| USP7 | 182 | IPI00003965.1 | 128272 |
| VAPA | 192 | IPI00170692.1 | 27318 |
| VESICULAR INTEGRAL-MEMBRANE PROTEIN VIP36 PRECURSOR | 234 | IPI00009950.1 | 40229 |
| VESICULAR-FUSION PROTEIN NSF. | 154 | IPI00006451.1 | 82654 |
| VLDL receptor | 29 | IPI00024273.1 | 96098 |
| VTRP | 155 | IPI00001643.1 | 72480 |
| Wolframin | 235 | IPI00008711.1 | 100306 |
| X11alpha | 115 | IPI00025752.1 | 92924 |
| X11beta | 74 | IPI00017817.1 | 82512 |

TABLE 3

BIOCHEMICAL ACTIVITIES OF THE COMPLEXES

| Name of Complex | Biochemical activity |
|-----------------------|--|
| APP-C59-complex | APP signaling activity (regulator of transcription) |
| Bace1-complex | APP processing beta-secretase |
| Bace2-complex | APP processing beta- and alpha-secretase |
| BRI-complex | Regulator of BRI and/or APP processing and/or signalling |
| Dab1-complex | Regulator of APP processing and/or signalling; Upstream activator of tau phosphorylation |
| Fe65L2-complex | Regulator of APP turnover, processing and signaling |
| Pilt-complex | Regulator of X11beta function and of APP processing and/or signalling |
| Paladin-complex | Regulator of X11beta function and of APP processing and/or signalling |
| Neurotrypsin-complex | Regulator of APP processing secretases |
| Hunc18a-complex | Regulator of secretory vesicular transport |
| Telencephalin-complex | Gamma-secretase activity and assembly (trafficking) |
| PC7-complex | Regulator of alpha- and beta-secretase activity |
| TFCP2-complex | Regulator of APP signaling activity (regulator of transcription) |
| Jip1-complex | Regulator of APP trafficking and signaling |
| Lamezin-complex | Regulator of protein glycosylation and phospholipid metabolism |
| VTRP-complex | Regulator of vesicular transport between endoplasmic reticulum and Golgi |

| | |
|---------|------------------------------|
| P75 NTR | Apoptosis related signalling |
| | |

TABLE 4

MEDICAL APPLICATIONS OF THE COMPLEXES

| Complex | Medical application |
|----------------|--|
| mDAB1 | neurodegenerative disease such as Alzheimer's disease; |
| JIP1 | neurodegenerative disease such as Alzheimer's disease and related disorders; |
| Fe65L2 | neurodegenerative disease such as Alzheimer's disease; cancer such as prostate cancer and breast cancer and skin cancer |
| Pilt/TJP4 | neurodegenerative disease such as Alzheimer's disease; inflammatory conditions such as ulcerative colitis, Crohn's disease and atherosclerosis |
| Neurotrypsin | neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders |
| Hunc18a | neurodegenerative disease such as Alzheimer's disease and related disorders |
| Telencephalin | neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders |
| PC7 | neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders; |
| VTRP | neurodegenerative disease such as Alzheimer's disease; |
| BACE1 (new) | neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders |
| BACE2 | neurodegenerative disease such as Alzheimer's disease; |
| PALADIN | neurodegenerative disease such as Alzheimer's disease; |

| | |
|------------|---|
| TFCP2 | neurodegenerative disease such as Alzheimer's disease; |
| p75 NTR | neurodegenerative disease such as Alzheimer's disease; |
| Lamezin | neurodegenerative disease such as Alzheimer's disease, congenital muscular dystrophy 1C and limb-girdle muscular dystrophy 2; |
| APP-C59 | neurodegenerative disease such as Alzheimer's disease; |
| BRII/ITM2B | neurodegenerative disease such as Alzheimer's disease and familial British dementia; |

The present invention is not to be limited in scope by the specific embodiments described herein. Indeed, various modifications of the invention in addition to those described herein will become apparent to those skilled in the art from the foregoing description and accompanying figures. Such modifications are intended to fall within the scope of the appended claims.

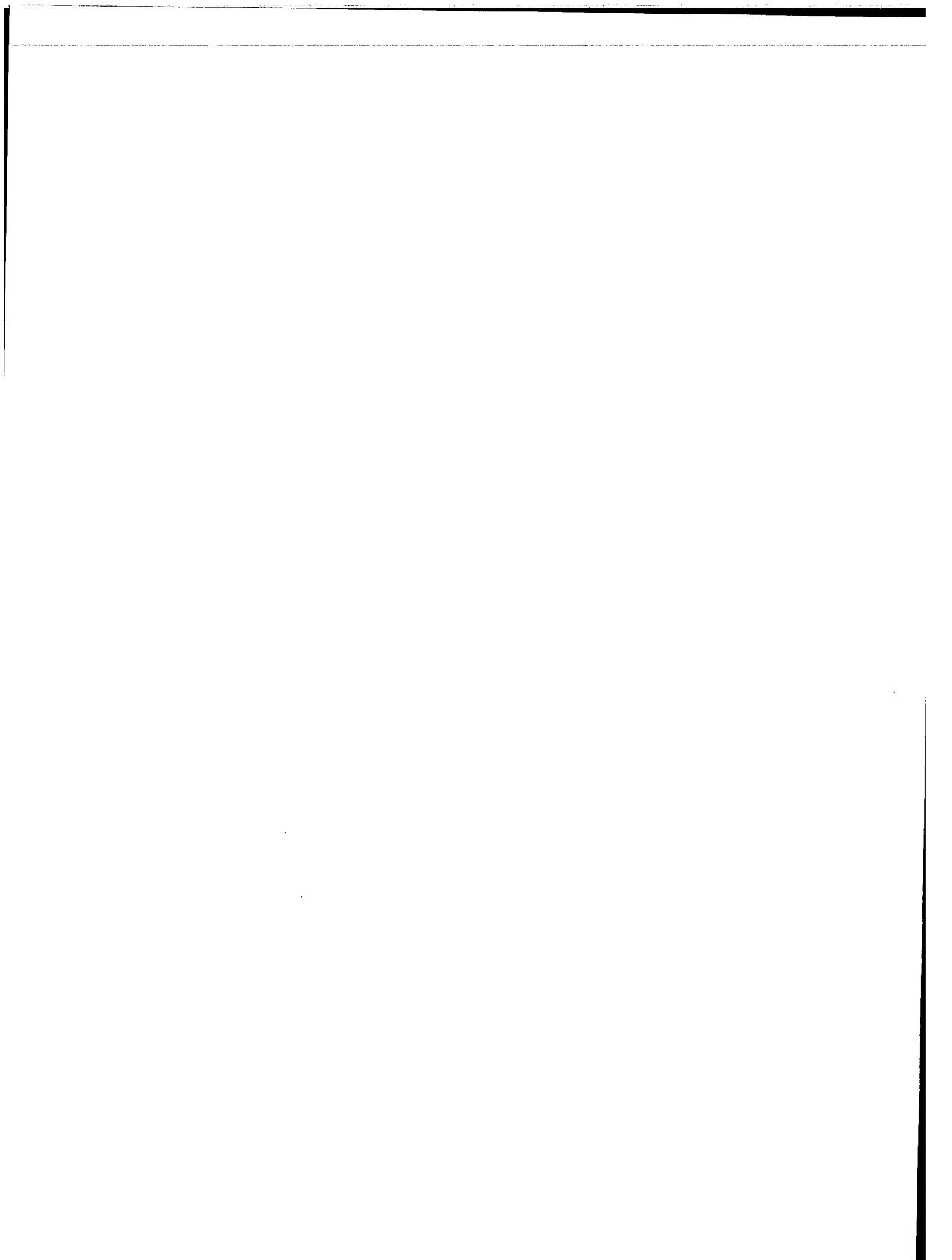
Various publications are cited herein, the disclosures of which are incorporated by reference in their entireties.

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SEQUENCES

29. Jan. 2004

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 LVRVAGKEKCVYFFWQGRHSTVSEKGT SALMTVELDEERGAQVQVLQGKEPPCFLQC
 FQGGMVVHSGRREEEEENVQSEWRLYCVRGEVPMEGNLLEVACHCSSLRSTSVMVV
 LNINKALIYLWHGCKAQGHTKEVGRTAANKIKEECPLEAGLHSSSNVTIHECDEGSEPLG
 FWDALGRRDRKAYDCMLQDPGSFNAPRLFILSSSGDFSATEFVYPAQAPS AVSSMP
 FLQEDLYSAPQPALFLVDNHHEVYLWQGWWPTENKITGSARIRWASDRKSAMETVLQ
 YCRGKNLKRPPP KSYLIHAGLEPLTFTNMFPSWEHREDIAEITEMDTEVSNQITLVEDVL
 AKLCKTIYPLADLLARPLPEGVDPLKLEIYLTDEDFEFAL DMSRDEFNALPTWKQVN LKK
 SKGLF

SEQ ID No:8

MAGNFDSEERSSWYWGRLSRQEAVALLQGQRHGVFLVRDSSTSPGDYVLSVSENSR
 VSHYIINSSGPRPPVPPSPAQPPPGVSPSRLRIGDQEFDSPALLEFYKIHYWDTTLIEP
 VSRSRQSGVILRQEEAEYVRALDFNGNDEEDLPFKKG DILRIRD KPEEQWWNAEDS
 EGKRG MIPV PYVEKYRPASASVSALIGGNQEGSHPQPLGPPEPGPYAQPSVNTPLPNL
 QNGPIYARVIQKRVPNAYDKTALALEVGELVKVT KINVSGQWE GGCGNGKRGHFPFTHV
 RLLDQQNPDED FS

SEQ ID No:9

MSSARFDSSDRSAWYMGPVSRQEATRLQGQRHGMFLVRDSSTCPGDYVLSVSENS
 RVSHYIINSLPNRRFKIGDQEFDHLPALLEFYKIHYLDTTLIEPAPRYPSPPMGSVSAPN
 LPTAEDNLEYVRTLYDFPGNDAEDLPFKKG EILVIIEKPEEQWW SARNKDGRVGMIPV P
 YVEKLV RSSPHGKHGNRNSNSYGIPEPAHAYAQPQTTPLPAVSGSPGAAITPLPSTQN
 GPVFAKAIQKRVPCAYDKTALALEVGDIVKVTRMNINGQWE GEVNGRKGLFPFTHVKIF
 DPQNP DENE

SEQ ID No:10

MELRVGNRYRLGRKIGSGSGFDIYLGT DIAAGEEEVAIKLECVKT KHPQLHIESKIYKMMQ
 GGVGIPTIRWCGAEGDYNVMVMELLGPSLEDLFNFC SRKFSLKTVLLADQMISRIEYIH
 SKNFIHRDVKP DNFLMGLGKKGNL VYIIDFGLA KKYRDARTHQHIPYRENKNLTGTARYA
 SINTHLGIEQSRRDDLES LGYVLMYFNLGSLPWQGLKAATKRQKYERISEKKMSTPIEVL

CKGYPSEFATYLNFCRSLRFDDKPDYSYLRLQLFRNLFRQGFSYDYVFDWNMLKFGAS
 RAADDAERERRDREERLRHSRNPATRGLPSTASGRLRGQTQEVAAPPTPLPTSHTANTS
 PRPVSGMERERKVSMRLHRGAPVNISSSDLTGRQDTSRMSTSQIPGRVASSGLQSVV
 HR

SEQ ID No:11

MELRVGNKYRLGRKIGSGSFGDIYLGANIASGEEVAIKLECVKTCHKPQLHIESKFYKMMQ
 GGVGIPSIKWCGAEGDYNVMVMELLGPSLEDLFNFCRSRKFSLKTVLLADQMISRIEYIH
 SKNFIHRDVKPDNFLMGLGKKGNLVYIIDFGLAKKYRDARTHQHIPYRENKNLTGTARYA
 SINTHLGIEQSRRDDLESLGYVLMYFNLngSLPWQGLKAATKRQKYERISEKKMSTPIEVL
 CKGYPSEFSTYLNFCRSLRFDDKPDYSYLRLQLFRNLFRQGFSYDYVFDWNMLKFGAA
 RNPEDVDRERREHEREERMGQLRGSATRALPPGPPTGATANRLRSAAEPVASTPASRI
 QPAGNTSPRAISRVDRERKVSMLHRGAPANVSSDLTGRQEVSRIQPASQTSVPFDHL
 GK

SEQ ID No:12

MKMWLLVSHLVIISITTCLAEFTWYRRYGHGVSEEDKGFGPIFEEQPINTIYPEESLEGKV
 SLNCRARASPFPVYKWRMNNGDVDLTSDRYSMVGGNLVINNPDQKDAGIYYCLASN
 NYGMVRSTEATLSFGYLDPFPEERPEVRVKEGKGMVLLCDPPYHFPDDLSYRWLLNE
 FPVFITMDKRRFVSQLNGNLYIANVEASDKGNYSCFVSSPSITKSVFSKIFIPLIPERTTK
 PYPADIVVQFKDVKYALMGQNVTLCECFALGNPVPDIRWRKVLEPMPTAEISTSGAVLKIF
 NIQLEDEGIYECEAENIRGKDKHQARIYVQAFPEWVEHINDTEVDIGSDLYWPCVATGKP
 IPTIRWLKNGYAYHKGELRLYDVTFENAGMYQCIAENTYGAIYANAELKILALAPTFEMN
 PMKKKILAAGGRVIIECKPKAAPKPKFSWSKGTEWLVNSSRILIWEDGSLEINNITRND
 GGIYTCFAENNNGKANSTGTLVITDPTRIILAPINADITVGENATMQCAASFDPALDLTFV
 WSFNGYVIDFNKENIHYQRNFMLDSNGELLIRNAQLKHAGRYTCTAQTVNDNSSASADL
 VVRGPPGPPGGLRIEDIRATSVALTWSRGSDNHSPISKYTQTKTILSDDWKDAKTDPII
 EGNMEAARAVDLIPWMEYEFRVVATNTLGRGEPSIPSNIKTDGAAPNVAPSDVGGGG
 GRNRELTTWAPLSREYHYGNFGYIVAFKPDFGEEWKKVTVTNPDGRTVHKDETMS
 PSTAFQVKVKAFNNKGDPYSLVAVINSAQDAPSEAPTEVGVKVLSSSEISVHWEHVLE
 KIVESYQIRYWAHDKEEAANRVQVTSQEYSARLENLLPDTQYFIEVGACNSAGCGPPS
 DMIEAFTKKAPPSPRISSVRSGSRYIITWDHVVALSNESTVTGYKVLYRPDGQHDGK
 LYSTHKHSIEVPIPRDGEYVVEVRAHSDGGDGVSQVKISGAPTLSPSLLGLLPAGFILV
 YLEF

SEQ ID No:13

MSTETELQAVAKTSACKDSRKKGQDRSEATLIKRFKGEGVRYAKLIGIDEVSAARGDK
 LCQDSMMKLGVVAGARSKGHEHKQKIFLTISFGGIKIFDEKTGALQHHHAVHEISYIAKDI
 TDHRAFGYVCGKEGNHRFVAIKTAQAAEPVILDRLFQLIYELKQREELEKKAQKDKQ
 CEQAVYQTILEEDVEDPVYQYIVFEAGHEPIRDPETEENIYQVPTSQQKEGVYDVPKSQ
 PVSAVTQLELFGDMSTPPDITSPPATPGDAFIPSSSQTLPASADVSSVPLGTAAVPP
 GYVAMGAVLPSFWGQQQPLVQQQMVMGAHPPVAQVMPGAQPIAWGQPGLFPATQQP
 WPTVAGQFPPAAFMPQTVMPL
 PAAMFQGPLTPLATVPGTSDSTRSPQTDKPRQKMGKETFKDFQMAQPPPVSRKPD
 QPSLTCTSEAFSSYFNKVGVAQDTDDCDDFDISQLNLTPVTSTTPSTNSPPTPAPRQSS
 PSKSSASHASDPTTDDIFEEGFESPKSEEQEAPDGSQASSNSDPFGEPSGEPSGDNI
 SPQDGDS

SEQ ID No:14

MPRLKESRSHESLLSPSSAVEALDLSMEEEVVIKPVHSSILGQDYCFEVTTSSGSKCFS
 CRSAAERDKWMENLRRAVHPNKNKDNRRVEHILKLWVIEAKDLPACKYLCELCLDDVL
 YARTTGKLKTDNVFWGEHFEFHNLPLRTVTVHLYRETDKKKKERNSYLGLVSLPAAS
 VAGRQFVEKWYPVVTPNPKGKGPGPMIRIKARYQTITILPMEMYKEFAEHITNHYLGL
 CAALEPILSAKTKEEMASALVHILQSTGKVKDFTLMMSEVDRCGDNEHLIFRENTLAT
 KAIEEYLKLVGQKYLQDALGEFIKALYESDENCEVDPSKCSAADLPEHQGNLKMCCCLA
 FCKIINSYCVFPRELKEVFASWRQECSSRGRPDISERLISASLFLRFLCPAIMSPSLFNLL
 QEYPDDRRTARTTLIAKVTQNLANFAKFGSKEEYMSFMNQFLEHEWTNMQRFLLEISNP
 ETLSNTAGFEGYIDLGRELSSLHSLLWEAVSQLEQSIVSKGLPLPRIIRDVHTALSTPGS
 GQLPGTNDLASTPGSGSSSISAGLQKMWENDLSGLIDFTRLPSPTPENKDLFFVTRSSG
 VQPSPARSSSYSEANEVDLQMANGKSLSMVDLQDARTLDGEAGSPAGPDVLPTDGQ
 AAAAQLVAGWPARATPVNLAGLATVRRAGQTTPGTSEGAPGRPQLLAPLSFQNPVY
 QMAAGLPLSPRGLGDSGSEGHSSLSSHSNSEELAAAALKGSFSTAEEELARRPGELAR
 RQMSLTEKGQPTVPRQNSAGPQRRIDQPPPPPPPPAPRGRTPPNLLSTLQYPRP
 SSGTLASASPDWVGPPSTRLRQQSSSSKGDSPELKPRAVHKQGPSPVSPNALDRTAAW
 LLTMNAQLLEDEGLGPDPPhRDRRLRSKDELSQAEKDLAVLQDKLRISTKKLEEYETLFK
 CQEETTQKLVLEYQARLEEGERLRRQQEDKDIQMKGIIISRLMSVEEELKKDHAEMQA
 AVDSKQKIIDAQEKRISLDAANARLMSALTQLKERYSMQARNGISPTNPTKLQITENGE
 FRNSSNC

SEQ ID No:15

MGKDYYQTLGLARGASDEEIKRAYRRQALRYHPDKNKEPGAEEKFKEIAEAYDVLSDP
RKREIFDRYGE EGLKGSGPSGGGGANGTSFSYTFHGDPHAMFAEFFGGRNPFDTF
FGQRNGEEGMDIDDPFSGFPMGMGGFTNVNFGRSRSAQE PARKKQDPPVTHDLRVS
LEIYSGCTKKMKISHKRLNPDGKSIRNEDKILTIEVKKGWKEGTKITFPKEGDQTSNIP
ADIVFVLKDKPHNIFKRDGSVDIYPARISLREALCGCTVNVTLDGRTIPVVFKDVIRPGM
RRKVPGEGLPLPKTPEKRGDLIIEFEVIFPERIPQTSRTVLEQVLPI

SEQ ID No:16

MGSPGASLGKIKALQSEQAT ALPASAPAVSQPTAPAPSCLPKAGQVIPALLREAPFSSVI
APTLLCGFLFLAWVAAEVPEESSRMAGSGARSEEGRRQHAFVPEPF DGANVVPNLWL
HSFEVINDLNHW DHITKLRLKESLRGEALGVYNRLSPQDQGDYGTVKEALLKA FGVPG
AAPSHLPKEIVFANS MGKGYYLKKGKIGKVPVRFLVDSGAQVSVVHPNLWEEVTDGDLD
TLQPFENVVKVANGAEMKILGVWDTAVSLGKLKLKAQFLVANASAEEAI GTDVLQDHN
AILDFEHRTCTLKGKKFRLLPVGGSLEDEFDLELIEEDPSSEEGRQELSH

SEQ ID No:17

MGDMGDPPKKRLLISLCVGCGNQIHDQYILRVSPDLEWHAACLKAECNQYLDESCTC
FVRDGKTYCKRDYIRLYGIKCAKCSIGFSKNDVMRARSKVYHIECFRCVACSRQLIPGD
EFALREDGLFCRADHDVVERASLGAGDPLSPLHPARPLQMAAEPI SARQPALRPHVHK
QPEKTTRVRTVLNEKQLHTLRTCYAANPRPDALMKEQLVEMTGLSPR VIRWFQN KRC
KDKKRSIMMKQLQQQPNDKTNIQGMTGTPMVAASPERHDGLQANPVEVQSYQPP
WKVLSDFALQSDIDQPAFQQLVNFS EGGPGSNSTGSEVASMSSQLPDTPNSMVASPIE
A

SEQ ID No:18

FNVDVKNSMTFSGPVEDMFGYT VQQYENE EGKWVLIGSPLVGQPKNRTGDVYKCPVG
RGESLPCVKLDLPVNTSIPNVTEVKENMTFGSTLV TNPNNGFLACGPLYAYRCGHLHYT
TGICSDVSPTFQVVNSIAPVQECSTQLDIVVLDGSNSIYPWDSVTAFLNDLLKRMDIGPK
QTQVGIVQYGENVTHEFNLNKYSSTEEVLVAKKIVQRGGRQTMTALGTD TARKEAFTE
ARGARRGVKKVMVITDGE SHDNHRLKKVIQDCEDENIQRFSIA ILGSYNRGNLSTEKFV
EEIKSIASEPTEKHFFNVSDELALVTIVKTLGERIFALEATADQSAASFEMEMSQTGFSAH
YSQDWVMLGAVGAYDWNGTVVMQKASQIIIPRNTTFNVESTKKNEPLASYLGYTVNSA

TASSGDVLYIAGQPRYNHTGQVIYRMEDGNIKILQTLSGEQIGSYFGSILTTDIDKDSNT
 DILLVGAPMYMGTEKEEQGKVYYVALNQTRFEYQMSLEPIKQTCCSSRQHNSCTTENK
 NEPCGARFGTAIAAVKDLNLDGFNDIVIGAPLEDDHGGAVYIYHGSGKTIRKEYAQRIPS
 GGDGKTLKFFGQSIHGEMLNGDGLTDVTIGGLGGAALFWSRDVAVVKVTMNFEPENKV
 NIQKKNCHMEGKETVCINATCFEVKLKSKEDETIYEADLQYRVTLDSLRQISRSFFSGTQ
 ERKVQRNITVRKSECTKHSFYMLDKHDFQDSVRITLDFNLDPENGVLDDSLPNSVHE
 YIPFAKDCGNKEKCISDLSLVATTEKDLLIVRSQNDKFNVSLTVKNTKDSAYNRTIVHY
 SPNLVFSGIEAIQKDSCESNHNITCKVGYFLRRGEMVTFKILFQFNTSYLMENVTIYSA
 TSDSEEPPETLSDNVVNISIPVKYEVGLQFYSSASEYHISIAANETVPEVINSTEIDIGNEINI
 FYLIRKSGSFPMPELKLSISFPNMTSNGYPVLYPTGLSSSENANCORPHIFEDPFSINSGK
 KMTTSTDHLKRGTILDNCNTCKFATITCNLTSSDISQVNVSILWKPTFIKSYFSSLNLIRG
 ELRSENASLVLSSSNQKRELAIQISKDGLPGRVPLWVILLSAFAGLLLLMLLLALWKIGFF
 KRPLKKKMEK

SEQ ID No:19

MNLQPIFWIGLISSVCCVFAQTDENRCLKANAKSCGEICIQAGPNCGWCTNSTFLQEGM
 PTSARCDDLEALKKKGCPPDDIENPRGSKDIKKNNVNRSKGTAEKLKPEDIHQIQPQ
 QLVLRLRSGEPQTTLKFKRAEDYPIDLYLMDLSYSMKDDLENVKSLGTDLMNEMRRI
 TSDFRIGFGSFVEKTVMPYISTTPAKLRNPCTSEQNCTTPFSYKNVLSLTNKGEVFNELV
 GKQRISGNLDSPEGFDAIMQVAVCGSLIGWRNVTRLLVFSTDAGFHAGDGKLGGIVL
 PNDGQCHLENNMYTMSHYYDYPSSIAHLVQKLSENNIQTIFAVTEEFQPVYKELKNLIPKS
 AVGTLSANSSNVIQLIIDAYNSLSSEVILENGKLSEGVTISYKSYCKNGVNGTGENGRKC
 SNISIGDEVQFEISITSNKCPKKDSDFKIRPLGFTEEVEVILQYICECECQSEGIPESPKC
 HEGNGTFECGACRCNEGRVGRHCECSTDEVNSEMDAYCRKENSSEICSNNGECVC
 GQCVCRKRDNTNEIYSGFCEDNFNCDRSNGLICGGNGVCKCRVCECNPNTGSAC
 DCSDLTSTCEASNGQICNGRGICECGVCKCTDPKFQGQTCEMCQTCLGVCAEHKECV
 QCRAFNKGEKKDTCTQECSYFNITKVESRDKLQPQVQPDPSHCKEKDVFDDCWFYFT
 YSVNGNNEVMHVVENPECPTGPDIPIVAGVVAGIVLIGLALLIWKLLMIIHDRREFAKF
 EKEKMNAKWDTGENPIYKSAVTVVNPKYEGK

SEQ ID No:20

MGPWGWLWTVALLAAAGTAGVDRCERNEFQCQDGKCISYKWVCDGSAECQDG
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NDPDCEGSDEWPQRGRLYVFQGDSSPCSAFEFHCLSGECIHSSWRCDDGGPDCKD
 KSDEENCAVATCRPDEFQCSDGNCIHGSRQCDREYDCKDMSDEVGVNVTLCEGP
 KFKCHSGECITLDKVCNMRDCRDWSDEPIKECGTNECLDNNGCShVCNDLKIGYEC
 LCPDFQLVAQRRCEDIDECQDPDTCQLCVNLEGGYKCQCEEGFQLDPHTKACKAV
 GSIAYLFFTNRHEVRKMTLDRSEYTSIPNLRNVVALTEVASNRIYWSDLSQRMICSTQ
 LDRAHGVSSYDTVISRDIQAPDGLAVDWIHSNIWTDSVLGTVSVADTKGVKRKTLFRE
 NGSKPRAIVVDPVHGFMYWTDWGTPAKIKKGGLNGVDIYSLVTENIQWPNGITLDLLSG
 RLYWVDSLHSISSIDVNNGNRKTILEDEKRLAHPFSLAVFEDKVFWTDIINEAIFSANRL
 TGSDVNLLAENLLSPEDMVLFHNLTQPRGVNWCERTTLSNGGCQYLCLPAPQINPHSP
 KFTCACPDGMILLARDMRSCLEAEAAVATQETSTVRLKVSSTAVRTQHTTRPVPDTS
 RLPGATPGLTTVEIVTMSHQALGDVAGRNEKKPSSVRALSIVLPIVLLVFLCLGVFLLW
 KNWRLKNINSINFDPVYQKTTEDEVHICHNQDGYSYPSRQMVSLEDDVA

SEQ ID No:21

MMEIQMDEGGGVVVYQDDYCSGSVMSERVSGLAGSIYREFERLIHCYDEEVVKELMPL
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 EKKELQIQVEHYEFQTRQLELAKNYADQISRLEERESEMKEYNALHQRHTEMIQTYV
 EHIERSKMQVGGNSQTESSLPGRSRKERPTSLNVFPLADGTVRAQIGGKLVPAGDH
 WHLSDLGQLQSSSYQCPQDEMSESGQSSAAATPSTTGTKSNTPTSSVPSAAVTPLN
 ESLQPLGDYVGSKNSKRAREKRDSRNMEVQTQEMRNVSIGMGSSDEWSDVQDIID
 STPELDMPETRLDRTGSSPTQGIVNKAFGINDSLHESLAGSEVIGDVDEGADLLG
 ETSAPSVSGMGKEVGNLLENSQLLETKNALNVVKNDLIAKVDQLSGEQEVLRGELEAA
 KQAKVKLENRIKELEELKRVKSEAIIRREPKEEAEDVSSYLCTESDKIPMAQRFFFTR
 VEMARVLMERNQYKERLMELQEAVRWTEMIRASREHPSVQEKKKSTIWQFFSRLFSSS
 SSPPPAKRPyPSVNIHYKSPTTAGFSQRRNHAMCPISAGSRPLEFFPDDDCTSSARRE
 QKREQYRQVREHVRNDDGRLQACGWSLPAKYKQLSPNGQEDTRMKNVPVYCRP
 LVEKDPTMKLWCAAGVNLSGWRPNEDDAGNGVKPAPGRDPLTCREGDGEPKSAHT
 SPEKKKAELPEMDATSSRVWILTSTLTTSKVVIIDANQPGTVVDQFTVCNAHVLCIISIP
 AASDSDYPPGEMFLDSDVNPEDPGADGVLAGITLVGCATRCNVPRSNCSSRGDTPVLD
 KGQGEVATIANGKVNPQSSTEEATEATEVPDPGPSEPETATLRPGPLTEHVFTDPAPTP
 SSGPQPGSENGPEPDSSSTRPEPEPSGDPTGAGSSAAPTMWLGAQNGWLYVHSAVA
 NWKKCLHSIKLKDSVLSLVHKGRVLVALADGTLAIFHRGEDGQWDLNSYHLMMDLGHP
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 GDGVWVSIRLDSTLRLYHAHTHQHLQDVIEPYVSKMLGTGKLGFSVRITALLVAGSR

LWVGTGNGVVISIPLTEVVLHRGQLLGLRANKTSPTSGETSGEGARPGGIHVYGDDSSDRA
 ASSFIPYCSMAQAQLCFHGRDAVKFFVSPGNVLATLNGSVDSPAEGPGPAAPASE
 VEGQKLRNVLVLSGGEGYIDFRIGDGEDDETEEGAGDMSQVKPVLSKAERSHIIWWQV
 SYTPE

SEQ ID No:22

MSKQQPTQFINPETPGYVGFGANLPNQVHRKSVKGFEFTLMVVGESGLGKSTLINSFL
 TDLYPERVIPGAAEKIERTVQIEASTVEIEERGVKLRLTVVDTPGYGDAINCRDCFKTIISYI
 DEQFERYLHDESGLNRRHIIDNRVHCCFYFISPFGHGLKPLDVAFMKAIHNKVNIVPVIK
 ADTTLKERERLKKRILDEIEEHNIKIYHLPDAESDEDEDFKEQTRLLKASIPFSVVGSNQL
 IEAKGKKVRGRILYPWGVVEVENPEHNDFLKLRTMLITHMQDLQEVTDQLHYENFRSER
 LKRGGRKVENEDMNKDQILLEKEAELRRMQEMIARMQAQMQMQMGGDGDGGALG
 HHV

SEQ ID No:23

MSAAVTAGKLARAPADPGKAGVPGVAAPGAPAAAPPAAKEIPEVLVDPRSRRRYVRGRF
 LGKGGFAKCFCISDADTKEVFAGKIVPKSLLLPHQREKMSMEISIHRSLAHQHVVGFG
 FFEDNDFVFVLELCRRRSLLHKRRKALTEPEARYYLQRQIVLGCQYLHRNRVIHRDLK
 LGNLFLNEDLEVKGDFGLATKVEYDGERKKTCGTPNYIAPEVLSKKGHSFEVDVWSIG
 CIMYTLVGKPPFETSCCLKETYLRKKNEYSIPKHINPVAASLIQKMLQTDPTARPTINELL
 NDEFFTSGYIPARLPITCLTIPPRFSIAPSSLPSNRKPLTVLNKGLENPLPERPREKEEP
 VVRETGEVVDCHLSMLQQLHSVNASKPSEGLVRQEEAEDPACIPFWVSKWVDYSD
 KYGLGYQLCDNSVGVLFNDSTRLILYNDGDSLQYIERDGTESYLTVSSHPSLMMKITLL
 KYFRNYMSEHLLKAGANITPREGDELARLPYLRTWFRTRSAILHLSNGSVQINFFQDHT
 KLILCPLMAAVTYIDEKRDFRTYRLSLEEYGCCKELASRLRYARTMVDKLLSSRSASNR
 LKAS

SEQ ID No:24

MGCVQCKDKEATKLTEERDGSLNQSSGYRYGTDPTPQHYPFGVTSIPNYNNFHAA
 GQGLTVFGGVNSSHTGTLRTRGGTGVTLFVALYDYEARTEDDSFHKGEKFQILNSST
 KKGGKEGPEPQEIRFAGRSIDLLEGNHVVDTRLVEGSADTQWMSEPQRHIHGLPDVNG
 KRWYFGKLRKDAERQLLSFGNPRGTFIRESETTKGAYSLSIRDWDDMKGDHVKH
 IRKLDNGGYYITTRAQFETLQQLVQHYSERAAGLCCRLVVPCHKGMPRLTDLSVKT
 WEIPRESLQLIKRLGNGQFGEVWMGTWNGNTKVAIKTLKPGTMSPESFLEEAQIMKKLK

HDKLVQLYAVVSEEPIYIVTEYMNKGSLLDFLKDGEGRALKLPNLVDMAAQVAAGMAYI
ERMNYIHRDLRSANILVGNGLICKIADFGLARLIEDNEYTARQGAKFPIKWTAPEAALYGR
FTIKSDVWSFGILLTELVTKGRVPYPGMNNREVLEQVERGYRMPCPQDCPISLHELMIH
CWKKDPEERPTFEYLQSFLLEDYFTATEPQYQPGENL

SEQ ID No:25

MDAEGLALLLPPVTLAALVDSWLREDCPGLNYAALVSGAGPSQAALWAKSPGVLAGQP
FFDAIFTQLNCQVSWFLPEGSKLVPVARVAEVRGPAHCLLGERVALNTLARCSGIASA
AAAAVEAARGAGWTGHVAGTRKTPGFRIVEKYGLLVGGAASHRYDLGGLVMVKDNH
VVAAGGVEKAVRAARQAADFALKVEVECSSLQEAVQAAEAGADLVLLDNFKPEELHPT
ATVLKAQFPSVAVEASGGITLDNLPQFCGPHIDVISMGMLTQAAPALDFSLKLFAKEVAP
VPKIH

SEQ ID No:26

MSELEKAMVALIDVFHQYSRGDKHKLKKSELKELINNELSHFLEEIKEQEVDKVMET
LDNDGDGECDFQEAFVAMVTTACHEFFEHE

SEQ ID No:27

MWAEAGLPRAGGGSQPPFRTFSASDWGLTHLVHEQTGEVYVGAVNRIYKLSGNLTL
LRAHVTGPVEDNEKCYPSSVQSCPHGLGSTDNVNKLLLLDYAANRLLACGSASQGIC
QFLRLDDLFKLGEPHHRKEHYLSSVQEAGSMAGVLIAGPPGQGQAKLFVGTPIDGKSE
YFPTLSSRRLMANEEDADMFGFVYQDEFVSSQLKIPSDTLSKFPADFIYYVYSFRSEQF
VYYLTQLDTQLTSPDAAGEHFFTSKIVRLCVDDPKFYSYVEFPIGCEQAGVEYRLVQD
AYLSRPGRALAHQLGLAEDEDVLFTVFAQGQKNRVKPPKESALCLFTLRAIKEKIKERIQ
SCYRGEGKSLPWLLNKELGINSPLQIDDDFCGQDFNQPLGGTVTIEGTPLFVDKDDG
LTAVAAYDYZRGRVVVFAGTRSGRIRKDLNSNPGRPALAYESVVAQEGSPLRDLVSPN
HQYLYAMTEKQVTRPVESCVQYTSCELCLGSRDPHCGWCVLHSICSRRDACERADE
PQRFAADLLQCVQLTVQPRNVSVTMSQVPLVLQAWNVPDLSAGVNCSFEDFTESESVL
EDGRIHCRSPSAREVAPIRGQGDQRVVKLYLKSSETGKKFASVDFVFYNCSVHQSC
SCVNGSFPCWCKYRHVCTHNVADCAFLEGDRVNVSEDCPQILPSTQIYVPVGVVKPITL
AARNLPQPQSGQRGYECLFHIPGSPARVTALRFNSSLQCQNSSSYEGNDVSDLPVN
LSVWNNGNFVIDNPQNIQAHLYKCPALRESCGLCLKADPRFECGWCVAEERRCSLRHHC
AADTPASWMHARHGSSRCTDPKILKSPETGPRQGGTRLITGENLGLRFEDVRLGVR
VGKVL CSPVESEYISAEQIVCEIGDASSVRAHDALVEVCVRDCSPHYRALSPKRFTFVTP

TFYRVSPSRGPLSGGTWIGSHLNAGSDVAVGGRPCSFSWRNSREIRCLTPPGQ
 SPGSAPIININRAQLTNPEVKNYTEDPTILRIDPEWSINSGGTLVTGTNLATVREPRI
 RAKYGGIERENGCLVYNDTTMCRAPSANPVRSPPELGERPDELGFVMDNVRSSLVL
 NSTSFLYYPDPVLEPLSPTGLLELKPPSPLIKGRNLLPPAPGNSRLNYTVLIGSTPC
 VSETQLLCEAPNLTGQHKVTVRAGGFESPGLQVYSDSLLTLPALIVGIGGGGGLLLVI
 VAVLIAYKRKSRDADRTLKRLQLQMDNLESRVALECKEAFALQTDIHELTNDLDGAGIP
 FLDYRTYAMRVLFPGIEDHPVLKEMEVQANVEKSLTFLGQLLTKHFLLTFIRTLEAQRS
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 MLTNWFTFLLYK
 FLKECAGEPLFMLYCAIKQQMEKGPIAITGEARYSLSEDKLIRQQIDYKTTLNCVN
 PEN
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 EDVTTKIDNDWKRLNTLAHYQVTDGSSVALVPKQT SAYNISNSSTFKSLSRYESMLRT
 ASSPDLSRSRTPMITPDLESGTKLWHLVKNHDHLDQREGDRGSKMVSEIYLTRLLATKG
 TLQKFVDDLFE TIFSTAHRGSALPLAIKYMFDFLDEQADKHQIHADVRHTWKSNCPLR
 FWVNVIKNPQFVFDIHKNSITDACLSVVAQTFMDSCSTSEHKLGDSPSNKLLYAKDIPN
 YKSWVERYYADIAKMPAISDQDMSAYLAEQSRLHLSQFNMSMSALHEIYSITKYKDEILA
 ALEKDEQARRQRLRSKLEQVVDTMALSS

SEQ ID No:28

MAQGLEVALTDLQSSRNNVRHHTEEITVDHLLVRRGQAFNLTYFRNRSFQPGLDNII
 FV
 VETEDAVYLDSEPQRQEYVMNDYGFYQGSKNWIRPCPWNYGQFEDKIIDICLKLLDKS
 LHFQTDPATDCALRGSPVYVSRVVCAMINSNDDNGVLNGNWSENYTDGANPAEW
 WTGS
 VAILKQWNATGCQPVRYGQCWWFAAVMCTVMRCLGIPTRVITNFDSGHDTDGN
 LIIDEY
 YDNTGRILGNKKDTIWNFHWWNECWMARKDLPPAYGGWQVLDATPQEMSNGVYCC
 GPASVRAIKEGEVDLYDTPFVFSMVNACMSWLVQGGKEQKLHQDTSSVGN
 FISTKS
 IQSDERDDITENYKYEEGSLQERQVFLKALQKLKARSFHGSQRGAELQPSRPT
 SLSQDS
 PRSLHTPSLRPSDVQVSLKFKLLDPPNMQDICFVLLALNMSSQFKDLKV
 NLSAQSL
 HDGSPLSPFWQDTAFITLSPKEAKTYPCKISYSQYSQYLSTD
 KLIRISALGEEKSSPEKIL
 VNKIITLSYPSITINVGAAVVNQPLSIQVIFSNPLSEQVEDCV
 LTVEGSGLFKKQQKVFLG
 VLKPQHQASIILETPFKSGQRQIQANMRSNKF
 DIKGYRN
 VYVDFAL

SEQ ID No:29

MGTSALWALWLLALCWAPRESGATGTGRKAKCEPSQFQCTNGRCITLLW
 KC
 CDGDED
 CVDGSDEKNCVKKTCAESDFVCNNGQCVPSRWKCDGDPDCEDGSDESPEQCHMRT

CRIHEISCGAHSTQCIPSWRCDGENDCDSGEDEENCGNITCSPDEFTCSSGRCISRNF
 VCNGQDDCSDGSDELDCAPPTCGAHEFQCSTSSCIPISWVCDDDADCSDQSDESLEQ
 CGRQPVIHTKCPASEIQCGSGECIHKKWRCGDGDPDCKDGSDEVNCPSRTCRPDQFEC
 EDGSCIHGSRQCNGIRDCVDGSDEVNCKNVNQCLPGPKFKCRSGECIDISKVCNQEQQ
 DCRDWSDEPLKECHINECLVNNGGCSHICKDLVIGYECDAAGFELIDRKTCGDIDECQ
 NPGICSQICINLKGGYKCECSRGYQMMLATGVCKAVGKEPSLIFTNRRDIRKIGLERKEYI
 QLVEQLRNTVALDADIAAQKLFWADLSQKAIFSAISDDKVGRHVKMIDNVYNPAAIAVDW
 VYKTIYWTDAASKTISVATLDGTKRKFLFNSDLREPASIAVDPLSGFVYWSDWGEPAKIE
 KAGMNGFDRRPLVTADIQWPNGITLDLIKSRLYWLDKLHMLSSVLDNGQDRRIVLKSL
 EFLAHPLALTIFEDRVYWDGENEAVYGANKFTGSELATLVNNLNDAQDIIVYHELVQPS
 GKNWCEEDMENGGCEYLCLPAPQINDHSPKYTCSCPSCGYNVEENGRDCQSTATTVTY
 SETKDTNTTEISATSGLVPGGINVTTAVSEVSVPKGTSAAWAILPLLLLVMMAVGGYLM
 WRNWQHKNMKSMNFDNPVYLTTEEDLSIDIGRHSASVGHTYPAISVVSTDDLA

SEQ ID No:30

MSAAEAGGVFHRARGRTLDAFPAAKESEWKGPFYFILGADPQFGLIKAWSTGDCDNG
 GDEWEQEIRLTEQAVQAINELNPKPFFVLCGDLIHAMPKWRTEQTEDLKRVLRADV
 RAIPLVLVSGNHIGNPTAETVEEFCRTWGDDYFSFWVGGVLFLVLNSQFYENPSKCP
 SLKQAQDQWLDEQLSIARQRHCQHAIVFQHIPLFLESIDEDEDDYYFNLSKSTRKELADKF
 IHAGVRVVFSGHYHRNAGGTYQNLDMVVSSAIGCQLGRDPHGLRVVVVTAEKIVHRYY
 SLDELSEKGIEDDLMDLIK

SEQ ID No:31

MESYDVIANQPVIDNGSGVIKAGFAGDQIPKYCFPNVGRPKHVRVMAGALEGDFIG
 PKAEEHRGLLSIRYPMEHGIVKDWNDMERIWQYVYSKDQLQTFSEEHPVLLTEAPLNP
 RKNRERAAEVFFETFNVPALFISMQAVALSLYATGRTTGVVLDSDGVTHAVPIYEGFAM
 PHSIMRIDIAGRDSRFLRLYLRKEGYDFHSSSEFEIVKAIKERACYLSINPQKDETLETE
 KAQYLPDGSTIEIGPSRFRAPELLFRPDLLIGEESEGIHEVLVFAIQKSDMDLRRTLFSNIV
 LSGGSTLFKGFGDRLLSEVKKLAPKDVKIRISAPQERLYSTWIGGSILASLDTFKKMWVS
 KKEYEEDGARSIHRKTF

SEQ ID No:32

MSNPRSLEEKYDMMSGARLALILCVTKAREGSEEDLDALEHMFRQLRFESTMKRDPTA
 EQFQEELEKFQQAIDSREDPVSCAFVVLMAHGREGFLKGEDGEMVKLENLFEALNNKN

CQALRAKPKVYIIQACRGEQRDPGETVGGDEIVMVIKDSPQTIPYTDALHVYSTVEGYI
 AYRHDKKGSCFIQTLVDVFTKRKGHILELLTEVTRRMAEAELVQEGKARKTNPEIQSTLR
 KRLYLQ

SEQ ID No:33

MMRQAPTARKTTTRPKPTRPASTGVAGASSLGPGSASAGELSSSEPSTPAQTPLA
 APIIPTPVLTSPGAVPPLPSPSKEEEGLRAQVRDLEEKLETLRKRAEDKAKLKELEKHKI
 QLEQVQEWSKMQEQQQADLQRRRKEARKEAKEALEAKERYMEEEMADTADAIEMATLD
 KEMAEERAESLQQEVEALKERVDELTTDLEILKAEIEEKSDGAASSYQLKQLEEQNAR
 LKDALVRMRDLSSSEKQEHVKLQKLMEKKNQELEVVRQQRERLQEELSQAESTIDELK
 EQVDAALGAEEMVEMLTDRLNLNEEKVRELRETVGDLEAMNEMNDELQENARETELEL
 REQLDMAGRVRREAQKRVEAAQETVADYQQTIKKYRQLTAHLQDVNRELTNQQEASV
 ERQQQPPPETFDFKIKFAETKAHAKAIEMELRQMEVAQANRHMSLLAFMPDSFLRPG
 GDHDCVLVLLLMPPRICKAELIRKQAQEKFELSENCSERPGLRGAAGEQLSFAAGLVYS
 LSLLQATLHRYEHALSQCSVDVYKKVGSLYPPEMSAHERSLDFLIELLHKDQLDETVNVE
 PLTKAIKYQHLYSIHLAEQPEDCTMQLADHIKFTQSALDCMSVEVGRLRAFLQGGQEA
 TDIALLLRDLETSCSDIRQFCKKIRRRMPGTDAPGIPAALAFGPQVSDTLLDCRKHTLWV
 VAVLQEVAAAAQLIAPLAENEGLLVAALEELAFKASEQIYGTPSSSPYECLRQSCNILIS
 TMNKLATAMQEGERYDAERPPSKPPPVELRAAALRAEITDAEGLGLKLEDRETVIKEKK
 SLKIKGEELSEANVRLSLLKKLDSAACKDADERIEKVQTRLEETQALLRKKEKEFEETMD
 ALQADIDQLEAEKAELKQRLNSQSKRTIEGLRGPPPSGIATVSGIAGEEQQRGAIPGQA
 PGSVPGPGLVKDSPLLLQQISAMRLHISQLQHENSILKGAQMKSASLPPPLHVAKLSHE
 GPGSELPAGALYRKTSQLLETLNQLSTHTHVVDITRTSPAAKSPSAQLMEQVAQLKSL
 DTVEKLKDEVLKETVSQRPGATVPTDFATFPSSAFLRAKEEQQQDDTVYMGKVTFS
 GFGQRHRLVLTQEQLHQLHSRLIS

SEQ ID No:34

MAGLTDLQRLQARVEELERWVYGGARGSRKVADGLVKVQVALGNISSKRERVKILY
 KKIEDLIKYLDPEYIDRIAIPDASKLQFILAEEQFILSQVALEQVNALVPMldsahikavpe
 HAARLQRQLAQIHIQQQAPWGVGVRDEAGSLVEDVGFAQFLSVLHFGPTGPVCNH

SEQ ID No:35

MPLYEGLGSGGEGTAVVIDLGEAFTKCGFAGETGPRCIIPSVIKRAGMPKPVRVVQYNIN
 TEELYSYLKEFIHILYFRHLLVNPRDRRVIIIESVLCPSHFRETLTRVLFKYFEVPSVLLAP

SHLMALLTLGINSAMVLDCGYRESLVLPIFLSASHLCRIPVLCNCWALPLGGKALHKE
 ETQLLEQCTVDTSVAKEQLPSVMGSVPEGVLEDIKARTCFVSDLKRGLKIQAQFNIDG
 NNERPSPPPNDYPLDGEKILHILGSIRDSVVEILFEQDNEEQSVATLILDSLIQCPIDTRK
 QLAENLVVIGGTMLPGFLHRLLAEIRYLVEKPKYKKALGKTFRIHTPPAKANCVAWL
 GAIFGALQDILGSRSVSKEYYNQTGRIPDWCSLNPPLEMMFDVGKTQPPLMKRAFST
 EK

SEQ ID No:36

MLPDFPSPSTWAPGLLLPSGPALLSPSVLQDSLGRSEQPHPICSFQDDFQEDEMIDD
 NEEEDDEEEEEEEEGDGEQQEGGDGPSEAPAPGPLIPSPSVEEPHKHRPTTLRLT
 TLGAQDSLNNNGFDLVRPASWQETALCSPAPEALRELPGPLPATDTGPGGAQSPVR
 PGCDCEGNRPAEPPAPGGTSPSSDPGIEADLRSRSSGGRRSSQELSSPGSDSED
 AGGARLGRMISISETELELSSDGGSSSSGRSSHNTNSIEASSPASEPEPPREPPRRP
 AFLPVGPDDTNSEYESGSESEPDLSEDADSPWLLSNLVSRMISEGSSPIRCPGQCLSPA
 PRPPGEPVSPAGGAAQDSQDPEAAAGPGGVELVDMETLCAPPAPAAPRPGPAQP
 GPCLFLSNPTRDTITPLWAAPGRAARPGRACSAACSEEDEEDDEEEEDAEDSAGSPG
 GRGTGPSAPRDASLVYDAVKYTLVVDEHTQLELVSLRRCAGLGHDSEEDSGGEASEEEE
 AGAALLGGGQVSGDTSPDSDLTFSKKFLNVFNSTSRSSTESFLSCLVNGEERE
 QTHRAVFRFIPRHPDELELDVDDPVLEAEEDDFWFRGFNMRTGERGVFPAFYAHAVP
 GPAKDLLGSKRSPCWVERFDVQFLGSVEVPCHQGNGILCAAMQKIATARKLTVHLRPP
 ASCDLEISLRGVKLSLSGGGPEFQRCSHFFQMKNISFCGCHPRNSCYFGFITKHPLLSR
 FACHVFVSQESMRPVAQSVGRAFLEYYQEHLAYACPTEDIYLE

SEQ ID No:37

MAERESGGGLGGGAASPPAASPFLGLHIASPPNFRTHDISLEEFEDEDLSEITDECGLSL
 QCKDTLSLRPPRAGLLSAGGGGAGSRLQAEMLQMDLIDATGDTPGAEDDEEDDEER
 AARRPGAGPPKAESGQEPASRGQQQSQQSQGPGSGDTYRPKRPTTLNLFPQVPRS
 QDTLNNNSLGKKHSWQDRVSRSSPLKTGEQTPPHEHICLSDDELPPQSGPAPTTDRGT
 STDSPCRSTATQMAPPGGPPAAPPGRGHSHRDRIHYQADVRLEATEEIYLTPVQRP
 PDAAEPTSAFLPPTESRMSVSSDPDAAYPSTAGRPHPSISEEEEGFDCLSSPERAEPP
 GGGWRGSLGEPPPPRASLSSDTALSYDSVKYTLVVDEHAQLELVSLRPCFGDYSDE
 SDSATVYDNCASVSSPYESAIGEEYEEAPRPQPPACLSEDSTPDEPDVHFSKKFLNV
 MSGRSRSSAESFGLSCIINGEEEQTHRAIFRFVPRHEDELELEVDDPLLVELQAED
 YWYEAYNMRTGARGVFPAYYAIETKEPEHMAALAKNSDWVDQFRVKFLGSVQPYH

KGNDVLCAAMQKIATTRRLTVHFNPSSCVLEISVRGVKIGVKADDSQEAKGNKCSHFF
 QLKNISFCGYHPKNNKYFGFITKHPADHRFACHVFVSEDSTKALAESVGRAFQQFYKQF
 VEYTCPTEDIYLE

SEQ ID No:38

MSRSKRDNNFYSVEIGDSTFTVLKRYQNLPIGSGAQGIVCAAYDAILERNVAIKKLSRP
 FQNQTHAKRAYRELVLMKCVNHKNIIGLLNVFTPQKSLEEFQDVYIVMELMDANLCQVIQ
 MELDHERMSYLLYQMLCGIKHLHSAGIHRDLKPSNIVVKSCTLKILDGLARTAGTSF
 MMTPYVVTRYYRAPEVILGMGYKENVDLWSVGCIMGEMVCHKILFPGRDYIDQWNKVI
 EQLGTPCPEFMKKLQPTVRTYVENRPKYAGYSFEKLFPDVLFPADSEHNKLKASQARD
 LLSKMLVIDASKRISVDEALQHPYINVWYDPSEAEAPPKIPDKQLDEREHTIEEWKELIY
 KEVMDLEERTKNGVIRGQPSPLAQVQQ

SEQ ID No:39

MADLAECKVVMCRFRPLNESEVNRGDKYIAKFQGEDTVVIASKPYAFDRVQSSTSQE
 QVYNDCAKKIVKDVEGYNGTIFAYGQTSSGKTHMEGKLHDPEGMGIIPRIVQDIFNYI
 YSMDENLEFHIIKVSYFEIYLDKIRDLLDVSKTNLSVHEDKNRVPYVKGCTERFVCSPDEV
 MDTIDEGKSNRHVAVTNMNEHSSRSHSIFLINVKQENTQTEQKLSGKLYLVLAGSEKV
 SKTGAEGAVLDEAKNINKSLSLALGNVISALAEGSTYVPYRDSKMTRILQDSLGGNCRTTI
 VICCSPSSSYNESETKSTLLFGQRAKTIKNTVCVNVELTAEQWKKKYEKEKEKNKILRNTI
 QWLENELNRWRNGETVPIDEQFDKEKANLEAFTVDKDITLTNDKPATAIGVIGNFTDAE
 RRKCEEEIAKLYKQLDDKDEEINQQSQLVEKLKTQMLDQEELLASTRRDQDNMQAELN
 RLQAENDASKEEVKEVLQALEELAVNYDQKSQEVEDKTKEYELLSDELNQKSATLASID
 AELQKLKEMTNHQKKRAAEMMASLLKDLAEIGIAVGNNNDVKQPEGTMIDEEFTVARLY
 ISKMKSEVKTMVKRCKQLESTQTESNKMEENEKELAACQLRISQHEAKIKSLTEYLQN
 VEQKKRQLEESVDALSEELVQLRAQEKVHEMEKEHLNKVQTANEVKQAVEQQIQSHRE
 THQKQISSLRDEVEAKAKLITDLQDQNQKMMLEQERLRVEHEKLKATDQEKSRLHELT
 VMQDRREQARQDLKGLEETVAKELOTLHNLRLFVQDLATRVKKSAEIDSDDTGGSAA
 QKQKISFLENNLEQLTKVHKQLVRDNADLRCELPKLEKRLRATAERVKALESALKEAKE
 NASRDRKRYQQEVDRIKEAVRSKNMARRGHSAQIAKPIRPGQHPAASPTHPSAIRGGG
 AFVQNSQPVAVRGGGGKQV

SEQ ID No:40

MSTMVYIKEDKLEKLTQDEIISKTKQVIQGLEALKNEHNSILQSLLETLKCLKKDDESNLV
EEKSNMIRKSLEMLELGLSEAQVMMALSNHLNAVESEKQKLRAQVRRLCQENQWLRD
ELANTQQQLQKSEQSVAQLEEEKKHLEFMNQLKKYDDDISPSEDKDSTKEPLDDLFP
NDEDPPGQGIQQQHQSSAAAAAQGGYEIPARLRTLHNLVIQYASQGRYEVAVPLCKQA
LEDLEKTSGHDPDVATMLNILALVYRDQNKYKDAANLLNDALAIREDTLGKDHPAVAAT
LNNLAVLYGKRGKYKEAEPLCKRALEIREKVLGKDHPDVAKQLNNLALLCQNQGKYEEV
EYYYQRALEIYQTKLGPDDPNVAKTKNNLASCYLKQGKFKAETLYKEILTRAHEREFG
SVDDENKPIWMHAEEERECKGKQKDGTSGEYGGWYKACKVDSPTVTTLKNLGALY
RRQGKFEAAETLEEAAMRSRKQGLDNVHKQRVAEVLDOPENMEKRRSRESLNVDVVK
YESGPDGGEEVSMSVEWNGGVSGRASFCGKRQQQWPGRHR

SEQ ID No:41

MADPAECSIKVMCRFRPLNEAEILRGDKFIPFKKGDETVVIGQGKPYVFDRVLPPNTTQE
QVYNACAKQIVKDVLEGYNGTIFAYGQTSSGKTHMEGKLHDPQLMGIIPRIAHIDIFDHIY
SMDENLEFHFIKVSYFEIYLDKIRDLLDVSKTNLAVHEDKNRVPYVKGCTERFVSSPEEV
DVIDEKGKANRHVAVTNMNEHSSRSHSIFLINIKQENVETEKKLSGKLYLVLAGSEKVK
TGAEGAVLDEAKNINKSLSALGNVISALAEGTKTHVPYRDSKMTRILQDSLGGNCRTTIVI
CCSPSVFNEAETKSTLMFGQRAKTIKNTVSVNLELTAEEWKKYEKEKEKNKTLKNVIQ
HLEMELNWRNRNGEAVPEDEQISAKDQKNLEPCDNTPIIDNIAPVVA
GISTEEKEKYDEEI
SSLYRQLDDKDEINQQSQLAEKLKQQMLDQDELLASTRRDYEKIQEELTRLQIENEAA
KDEVKEVLQALEELAVNYDQKSQEVEDKTRANEQLTDELAQKTTLT
TQRELSQLQEL
SNHQKKRATEILNLLKDLGEIGGIIGTNDVKT
LADVNGVIEEEFTMARLYISKMKSEVKSL
VNRSKQLESQMDSNRKMNASERELAACQLLISQHEAKIKSLTDYMQN
MEQKRRQLEE
SQDSLSEELAKLRAQEKMHEVSFQDKEKEHLTRLQDAEEMKKALEQQ
MESHREAHQK
QLSRLRDEIEEKQKIIDEIRDLNQKLQLEQEKLSSDYNKL
KIEDQEREMKLEKLLLNDKR
EQAREDLKGLEETVSRELQTLHNLRKLFVQDLT
TRVKKSV
ELDNDGGGSAAQKQKISF
LENNLEQLTKVHKQLVRDNADLRCELPKLEKRLRATA
ERVKALESALKEAKENAMRDRK
RYQQEVDR
IKEAVRAKNMARRAHS
AQIAKPIRPGHYPASSPTAV
HAIRGGGGSSNST
HYQK

SEQ ID No:42

MPGPASPAARGLSRRPGQPPLPLLLPLLLLLRAQPAIGSLAGGSPGAAEAPGSAQVAGL
CGRLTLHRDLRTGRWE
PDPQRSRRCLRDPQRVLEYCRQMYP
ELQIARVEQATQAIPM
ERWCGGSRSGSCAHPHHQVVPFRCLP
GEFVSEALLVPEGCRFLH
QERMDQCESSTR

RHQEAQEACSSQGLILHGSGMILLPCGSDRFRGVEYVCCPPPGTPDPSGTAVGDPSTR
 SWPPGSRVEGAEDEEEEESFPQPVDDYFVEPPQAEEEEETVPPPSSHTLAVVGKVTP
 PRPTDGVDIYFGMPGEISEHEGFLRAKMDLEERRMRQINEVMREWAMADNQSKNLPK
 ADRQALNEHFQSILQTLEEQQVSGERQRQLVETHATRVLINDQRRAALEGFLAALQADPP
 QAERVLLALRRYLRAEQKEQRHTLRHYQHVAADVPEKAQQMRFQVHTHLQVIEERVN
 QSLGLLDQNPHLAQELRPQIQELLHSEHGPSELEAPAPPGSSEDKGGLQPPDSKDDT
 PMTLPKGSTEQDAASPEKEKMNPLEQYERKVNASVPRGFPHSSEIQRDELAPAGTGV
 SREAVSGLLIMGAGGGSLIVLSMLLLRRKKPYGAISHGVVEVDPMLTLEEQQQLRELQRH
 GYENPTYRFLEERP

SEQ ID No:43

AGARRRRGRGGEAPLLPGLAAAEPRAWRDPGLAEPAVRGRRVGSGPRGTMSAKVRLK
 KLEQLLLDGPWRNESALSvetLLDVLCLYTECSHSALRRDKYVAEFLWAKPFTQLVK
 EMQLHREDFEIIVIGRGAFFGEAVVVKMKNTERIYAMKILNKWEMLKRAETACFREERD
 VLVNGDCQWITALHYAFQDENHLYLVMDYYVGGDLTLLSKFEDKLPEDMARFYIGEMV
 LAIDSIHQLHYVHRDIKP DNVLVCLYTECSHSALRRDKYVAEFLWAKPFTQLVK
 EILQAMEDGMGKYGPECWWSLGVC MYEMLYGETPFYAESL VETYGKIMNHEERFQF
 PSHVTDVSEEAKDLIQRRLICSERRLGQNGIEDFKKHAFFEGLNWENIRNLEAPYIPDVS
 SPSDTSNFDVDDDVLRNTEILPPGSHTGFSGLHLPFIGFTTDESCFSDRGSLKSIMQSN
 TLTKDEDVQRDLEHSLQMEAYERRIRRLEQEKELESRKLQESTQTVQSLHGSSRALNS
 NRDKEIKLNEEIERLKNKIADSNRLERQLEDTVALRQEREDSTQRLRGLEKQHRVV
 RQ EKEELHKQLVEASERLKSQAKELKDAHQQRKLALQESELNERMAELRAQKQKVSRQL
 RDKEEEEMEVATQKVDAMRQEMRRAEKLKELEAQQLDDAVA
 EASKERKLREHSENFC
 QMESELEALKVKQGGRGAGATLEHQQEISIKKSELEKKVLFYEEELVRREASHVLEVKN
 VKKEVHDSESHQLALQKEILMLKDKLEKSKRERHNEMEEAVGTIKDYERERAMLFDEN
 KKL

TAENEKLCFVDKLTAQNRQLEDELQDLAAKESVAHWEAQIAEIIQWVSDEKDARGYL
 QALASKMTEELEALRSSSLGSRTLDPLWKVRRSQKLDMSARLELQSALEAEIRAKQLVQ
 EELRKVVDANLTLESKLKDSEAKNRELLEMEILKKMEEKFRADTGLKLPDFQDSIFEY
 FNTAPLAHDLTFRTSSASEQETQAPKPEASPSMSVAASEQQEDMARPPQRPSAVPLPT
 TQALALAGPKPKAHQFSIKSFSSPTQCSHCTSLMVGLIRQGYACEVCSFACHVSCKDG
 APQVCPPIPPEQSKRPLGVQVRGIGTAYKGHVVKPKPTGVKKWQRAYAVVCDCKLFL
 YDLPEGKSTQPGVIASQVLDLRDEFVSSVLASDVIHATRRDIPCIFRVTASLLGAPS
 KTTSSLLILTENENEKKWVGILEGLQSLHKNRLRNQVHVPLEAYDSSLPLIKAILTAAIVDA

DRIAVGLEEGLYVIEVTRDVIVRAADCKVHQIELAPREKIVILLCGRNHHVHLYPWSSL
 GAEGSFDIKLPETKGQCLMATATLKRNSGTCLFVAVKRLILCYEIQRTPHRKFNEIVAP
 GSVQCLAVLRDRLCVGYPMSGFCLLSIQGDGQPLNLVPNDPSLAFLSQQSFDALCAVEL
 ESEEVLLCFSHMGLYVDPQGRRARAQELMWPAAPVACSCSPHTVTYSEYGVDFDV
 RTMEWVQTIGLRRIRPLNSEGTLNLLNCEPPRILYFKSKFSGAVLNVPDTSDNSKKQML
 RTRSKRRFVFVPEEERLQQRREMLRDPELRSKMISNPTNFNVAHMGPGDGMQVLM
 DLPLSAVPPSQEERPGPAPTNLARQPPSRNKPYISWPSSGGSEPSVTVPLRSMSDPDQ
 DFDKEPDSDSTKHSTPSNNSNPSGPPSPNSPHRSQPLEGLEQPACDT

SEQ ID No:44

MPVAVMAESAFSFKLLDQCENQELEAPGGIATPPVYGQLLALYLLHNDMNNARYLWK
 RIPPAIKSANSELGGIWSVGQRIWQRDFPGIYTTINAHQWSETVQPIMEAIRDATRRRAF
 ALVSQAYTSIIADDFAAFVGLPVEEAVKGILEQGWQADSTTRMVLPRKPVAGALDVSFN
 KFIPLSEPAPVPPIPNEQLARLTDYVAFLEN

SEQ ID No:45

MAAAVRQDLAQLMNSSGSHKDLAGKYRQILEKAIQLSGAEQLEALKAFVEAMVNENVS
 LVISRQLLTDFCTHLPNLPDSTAKEIYHFTLEKIQPRVISFEEQVASIRQHLASIYEKEEDW
 RNAAQVLVGIPLLETGQXXQYNVDYKLETYLKIAIRLYLEDDDPVQAEAYINRASLLQNEST
 NEQLQIHYKVCYARVLDYRRKFIEAAQRYNELSYKTIVHESERLEALKHALHCTILASAG
 QQRSRMLATLFKDERCQQLAAYGILEKMYLDRIIRGNQLQEFAAMLMQHQKATTADGS
 SILDRAVIEHNLLSASKLYNNITFEELGALLEIPAAKAEKIASQMITEGRMNGFIDQIDGIVH
 FETREALPTWDKQIQSLCFQVNNLLEKISQTAPEWTAQAMEAQMAQ

SEQ ID No:46

MSAEVKVTGQNQEQQFLLLAKSAGAALATLIHQVLEAPGVYVFGELLDMPNVRELAESD
 FASTFRLLTVFAYGTYADYLAEARNLPPTEAQKNKLRHLSVVTAAVKCIPYAVLLEAL
 ALRNVRQLEDLVIEAVYADVLRGSLDQRNQRLEVDSIGRDIQRQDLSAIARTLQEWCV
 GCEVVLSGIEEQVSRANQHKEQQQLGLKQQIESEVANLKKTIVTAAAAAATSQDPEQH
 LTELREPAPGTNQRQPSKKASKGKGLRGSAKIWSKSN

SEQ ID No:47

MASALEQFVNSVRQLSAQGQMTQLCELINKSGELLAKNLSHLDTVLGALDVQEHSLGVL
 AVLFWKFSMPSVPDFETLFSQVQLFISTCNGEHIRYATDTFAGLCHQLTNALVERKQPLR

GIGILKQAIKMQMNTNQLTSIHADLCQLCLLAKCFCKPALPYLDVDMMDICKENGAYDAK
 HFLCYYYYGGMIYTGLKNFERALYFYEQAITTPAMAVSHIMLESYKKYILVSLILLGKVQQ
 LPKYTSQIVGRFIKPLSNAYHELAQVYSTNNPSELRLVNKHSETFTRDNNMGLVKQCL
 SSLYKKNIQRLTKTFLTLSLQDMAASRVQLSGPQEAEKYVLHMIEDGEIFASINQKDGMVS
 FHDNPEKYNNPAMLHNIDQEMLKCIELDERLKAMDQEITVNPQFVQKSMGSQEDDSGN
 KPSSYS

SEQ ID No:48

MAASGSGMAQKTWELANNMQUEAQSIDEIYKYDKKQQQEILAANLGTKDHHYFKYCKIS
 ALALLKMVMHARSGGNLEVMGLMLGKVDGETMIIMDSFALPVEGTETRVNAQAAAYEY
 MAAYIENAKQVGRLENAIGWYHSHPGYGCWLSGIDVSTQMLNQQFQEPFVAVVIDPTR
 TISAGKVNLngAFRTYPKGYPDPSEYQTIPNKIEDFGVHCKQYYALEVSYFKSSL
 RKLLELLWNKYWVNTLSSSLLTNADYTTGQVFDLSEKLEQSEAQLGRGSFMLGLETH
 DRKSEDKLAKATRDSCKTTIEAIHGLMSQVIKDKLFNQINIS

SEQ ID No:49

MACGVTGSVALHPLVILNISDHWIRMRSGEGRPVQVIGALIGKQEGRNIEVMNSFELL
 SHTVEEKIIDKEYYYTKEEQFKQVFKELEFLGWYTTGGPPDPSDIHVHKQVCEIIESPLF
 LKLNPMTKHTDLPVSFESVIDIINGEATMLFAELTYTLATEEAERIGVDHVARMTATGSG
 ENSTVAEHLIAQHSAIKMLHSRVKLILEYVKASEAGEVPFNHEILREAYALCHCLPVLSTD
 KFKTDFYDQCNDVGLMAYLGTITKTCNTMNQFVNKFNVLYDRQGIGRRMRGLFF

SEQ ID No:50

MAGEQKPSSNLLEQFILLAKGTSGSALTALISQVLEAPGVYVFGELLELANVQELAEGAN
 AAYLQLLNLFAYGTYPDYIANKESLPELSTAQQNKLKHLTIVSLASRMKCIPYSVLLKDLE
 MRNLRELEDLIEAVYTDIIQGKLDQRNQLLEVDFCIGRDIRKKDINNIVKTLHEWCDGCE
 AVLLGIEQQVLRANQYKENHNRTQQQVEAEVTNIKKTLKATASSSAQEMEQQLAEREC
 PPHAEQQRQPTKKMSKVKGVLVSSRH

SEQ ID No:51

MSNLSKGTSRKDTKMRIRAFPMDEKYVNSIW DLLKNAIQEIQRKNNSGLSFEELYR
 NAYTMVLHKHGEKLYTGLREVVTEHLINKVREDVLSLNNNFLQTLNQAWNDHQTA
 MIRDILMYMDRVYVQQNNVENVYNLGLIIFRDQVVRYGCIRDHLRQTLLDMIARERKGEV
 VDRGAIRNACQMLMILGLEGRSVYEEDFEAPFLEMSAEFFQMESQKFLAENSASVYIKK

VEARINEEIERVMHCLDKSTEPIVKVVERELISKHMKTIVEMENSGLVHMLKNGKTEDL
 GCMYKLFSRVPNGLKTMCECMSSYLREQGKALVSEEGEGKNPVDYIQGLLDLKSRFDR
 FLLESFNNDRLFKQTIAQDFEYFLNLNSRSPEYLSFIDDKLKKGVKGLTEQEVTILDKA
 MVLFRFMQEKFVFERYYKQHLARRLLTNKSVSDDSEKNMISKLKTECGCQFTSKLEGM
 FRDMSISNTTMDEFRQHLQATGVSLGGVDLTVRLTTGYWPTQSATPKCNIPPAPRHA
 FEIFRRFYLAHKHSQRQLTLQHHMGSADLNATFYGPVKKEDGSEVGVGGAQVTGSNTRK
 HILQVSTFQMFTILMFNNREKYTFEEIQQETDIPERELVRALQSLACGKPTQRVLTKEPK
 SKEIENGHIFTVNDQFTSKLHRVKIQTVAAKQGESDPERKETRQKVDDDRKHEIAAIVRI
 MKSRKKMQHNVLVAEVTTQQLKARFLPSPVVIKKRIEGLERELYARTPEDRKVYTYVA

SEQ ID No:52

MSQFKRQRINPLPGGRNFSGTASTSLLGPPPGLLTPPVATELSQNARHLQGGEKQRVF
 TGIVTSLHDYFGVVDEEVFFQLSVVKGRLPQLGEKVLVKAAYNPGQAVPWNAVKVQTL
 SNQPLLKSPAPPLLHVAALGQKQGILGAQPQLIFQPHRIPPLFPQKPLSLFQTSHLHS
 HLNRFPARGPHGRLDQGRSDDYDSKKRKQRAGGEWGAKKPRHDLPPYRVHLTPYT
 VDSPICDFLELQRRYRSLLVPSDFLSVHLSWLSAFPLSQPFSLHHPSRIQVSSEKEAAPD
 AGAEPIADSDPAYSSKVLLSSPGLEELYRCCMLFVDDMAEPRETPEHPLKQIKFLLGR
 KEEEAVLVGGEWSPLDGLDPQADPQVLVRTAIRCAQAQTGIDLSCGCKWWRFAEFQ
 YLQPGPPRRLQTVVVYLPDVWTIMPTLEEWEALCQQKAAEAAPPTQEAQGETEPTEQQA
 PDALEQAADTSRRNAETPEATTQQETDTLPEAPPPLPEPAVIARPGCVNLSLHGIVED
 RRPKERISFEAGVMVLAELFLEMLQRDFGYRVYKMLLSPKEVVSPPPEKEEAAKEEA
 TKEEEAIKEEVVKEPKDEAQNEGPACEAPLKEKGLLPKPLSSGGEEEEKPRGEASED
 LCEMALDPELLLRDDGEEEFAGAKLEDSEVRSVASNQSEMEFSSLQDMPKELDPSAV
 LPLDCLLAFVFFDANWCGYLHRRDLERILLTGIRLSAEQAKQLVSRVVTQNICQYRSLQ
 YSRQEGLDGGLPEEVLFGNLDLLPPPGKSTKPGAAPTEHKALVSHNGSLINVGSLLQRA
 EQQDSGRILYLENKIHTLELKLEESHNRFSATEVTNKTAAEMQELRVRLAEAEETARTA
 ERQKSQLQRLLQELRRRLTPQLEIQRVVEKADSWVEKEEPAPS

SEQ ID No:53

MLGKDYMIALIILVNCDSDLWGDHSLEVEAGLPPGWRKIHDAAAGTYYWHVPSGSTQWQ
 RPTWELGDAEDPGTGTEGIWGLRPPKGRSFSSLESSLDRSNNSLWYGGESYIQSMEP
 GAKCFAVRSLGWVEVPEEDLAPGKSSIAVNNCIQQLAQTRSRSQPPDGAWGEGQNML
 MILKKDAMSLVNPLDHSLIHCQPLVHIRVWVGSSKGRDRDFAFVASDKDSCMLKCHV
 FRCDVPAKAIASALHGLCAQILSERVEVSGDASCCSPDPISPEDLPRQVELDAVSQAA

QKYEALYMGTLPTVKAMGMDVLNEAIGTLTARGDRNAWVPTMLSVDSDSLMTAHPHQAE
 ASTEEEPLWQCPVRLVTFIGVGRDPHTFGLIADLGRQSFQCAFWCQPHAGGLSEAVQ
 AACMVQYQKCLVASAARGKAWGAQARARLRLKRTSSMDSPGGPLPLPLLKGGVGGA
 GATPRKRGVFSFLDAFRLKPSLLHMP

SEQ ID No:54

MDTSRLGVLLSLPVLLQLATGGSSPRSGVLLRGCPTHCHCEPDGRMLLRVDCSDLGLS
 ELPSNLSVFTSYLDLSMNNISQLLPNPLPSLRFLEELRLAGNALTYPKGAFTGLYSLKVL
 MLQNNQLRHVPTEALQNLRSLSQLRLDANHISYVPPSCFSGLHSLRHLWLDDNALTEIP
 VQAFRSLSALQAMTLALNKIHHIPDYAFGNLSSLVVLHLHNNRIHSLGKKCFDGLHSLET
 LDLNYYNLDEFPTAIRTLSNLKELGFHSNNIRSIPEKAFCVGNPSSLTIHFYDNPIQFVGRSA
 FQHLPELRTLTLNGASQITEFPDLTGTANLESLTGTGAQISSLPQTVCNQLPNLQVLDLSY
 NLLEDLPSFSVCQKLQKIDLRHNEIYEIKVDTFQQQLSLRSLNLAWNKIAIIHPNAFSTLPS
 LIKLDLSSNLLSSFPITGLHGLTHLKTGNHALQSLISSENFPELKVIEMPYAYQCCAFGV
 CENAYKISNQWNKGDNSSMDDLHKKDAGMFQAQDERDLEDFLDFEEDLKALHSVQC
 SPSPGPFKPCEHLLDGWLIRIGVWTIAVLALTNCALVTSTVFRSPLYISPIKLLIGVIAVN
 MLTGVSAAVLAGVDAFTFGSFARHGAWWENGVGCHVIGFLSIFASESSVFLLTAALE
 GFSVKYSAKFETKAPFSSLKVIIILCALLALTMAAVPLLGGSKYGASPLCLPLFGEPESTM
 GYMVALILLNSLCFLMMTIAYTKLYCNLDKGDENIWDCSMVKHIAALLFTNCILNCPVAF
 LSFSSLINLTFISPEVIKFILLVVVPLPACLNPLLYILFNPHFKEDLVS LRKQTYVWTRSKHP
 SLMSINSDDVEKQSCDSTQALVTFTSSSITYDLPPSSVPSPAYPVTESCHLSSVAFVPCL

SEQ ID No:55

MEVDGTPRRGGCKMPLPVQVFNLQGAVEPMQIDVDPQEDPQNAPDVNYVVENPSLDL
 EQYAASYSGLMRIERLQFIADHCPTLRVEALKMALSFVQRTFNVDMYEEIHRKLSEATR
 ELQNAPDAIPESGVVEPPALDTAWVEATRKKALLKLEKLDLKNYKGNSIKESIRRGHDD
 LGDHYLDGDLDSNALKCYSRARDYCTS AKHVINMCLNVIKVSYLVQNWSHVLSYVSKA
 ESTPEIAEQRGERDSQTQAILTKLKAAGLAELAARKYKQAAKCLLLASFHDCDFPELLS
 PSNVAIYGLCALATFDRQELQRNVISSSSFKLFL ELEPQVRDIIFKFYESKYASCLKMLD
 EMKDNLLLDMYLAPHVRTLYTQIRNRALIQYFSPYVSADMHRMAAFNTTVAALEDELT
 QLILEGLISARVDSHSKILYARDVDQRSTT FEKSLLMGKEFQRRAKAMMLRAAVLRNQIH
 VKSPPREGSQGELTPANSQSRMSTNM

SEQ ID No:56

RRRRPSSSRRLRGRGAAQMACPALGLEALQPLQPEPPPEPAFSEAQKWIEQVTGRSF
 GDKDFRTGLENGILLCELLNAIKPGLVKKINRLPTPIAGLDNIILFLRGCKELGLKESQLFD
 PSDLQDTSNRVTVKSLDYSRKLKNVLVTIYWLGAANSCTSYSGTTLNLKEFEGLLAQM
 RKDTDDIESPKRSIRDGYIDCWDSERSDSLSPPRHGRDDSFDSLDSFGSRSRQTPSP
 DVVLRGSSDGRGSDSESDLPHRKLPDVKKDDMSARRTSHGEPKSAVPFNQYLPNKSN
 QTAYVPAPLRKKKAEREELYRKSWSTATSPLGGERPFRYGPRTPVSDAESTSMFDMR
 CEEEAAVQPHSRARQEQLQLINNQLREEDDKWQDDLARWKSRRRSVSQDLIKKEER
 KKMEKLLAGEDGTERRSIKYREIVQEKEERRERELHEAYKNARSQEEAEGILQQYIE
 RFTISEAVLERLEMPKILERSHSTEPNLSSFLNDPNPMKYLRQQSLPPPFTATVETTIAR
 ASVLDTSMSAGSGSPSKTVTPKAVPMLTPKYSQPKNSQDVLFKVDGKVSVNGETV
 HREEEKERECPTVAPAHSLTKSQMFEVARVHGSPELKQDNNGSIEINIKPNSVPQEL
 AATTEKTEPNSQEDKNDGGKSRKGNIELASSEPQHFTTVTRCSPTVAFVEFPSSPQLK
 NDVSEEKDQKKPENEMSGKVELVLSQVKVKPKSPEPEATLTFPFLDKMPEANQLHLPN
 LNSQVDSPSSEKSPVTPQFKFWADPEEERRQEKWQQEQERLLQERYQKEQDKL
 KEWEKAQKEVEEEEERRYEEERKIIEDTVVPFTVSSSSADQLSTSSMTEGSGTMNKI
 DLGNCQDEKQDRRWKSFQGDDSDLLLKTRESDRLEEKSLTEGALAHSGNPVSKG
 HEDHQLDTEAGAPHCGTNPQLAQDPSQNQQTSNPTHSEDVKPKTLPLDKSINHQIES
 PSERRKKSPREHFQAGPFSPCSPTPPGQSPNRSISGKKLCSSCGLPLGKGAA
 MIIETLN
 LYFHIQCFRCGICKGQLGDAVSGTDVRIRNGLNCNDCYMRSRSAGQPTT

SEQ ID No:57

MLIKVKTGTKEIEIDIEPTDKVERIKERVEEKEGIPPQQQRILYSGKQM
 NDEKTAADYKIL
 GGSVLHLVLALRGGGGLRQ

SEQ ID No:58

MVPEAWRSGLVSTGRVVGVL
 LLLGALNKASTVIHYEIPEEREKGFAVGNVVANLGLDLG
 SLSARRFRVVSGASRRFFEVNRETGEMFVNDRLDREELCGTLP
 SCTVTL
 ELELV
 VVENPLEL
 FSVEVVIQDINDNNPAFPTQEMKLEISEAVAPGTRFPLESAHD
 PDVGNSNLS
 LQTYELSRN
 EYFALRVQTREDSTKYAELVLERALDREREPSLQLV
 LTALDGGTP
 ALSASLPIHIKV
 VLDA
 ND
 NAPVFNQSLYRARVLEDAPS
 GTRVQVL
 ATDL
 DEGPNGE
 IIYSFGSHNRAGVRQLF
 AL
 LD
 LVTGMLTIKGR
 LDFEDTKL
 HEIYIQAKD
 KGANPEGA
 HCKVL
 VE
 VDV
 ND
 NAPEIT
 TV
 SVYSPV
 PEDAPL
 GTVIAL
 LS
 VTD
 LDAG
 ENGL
 VTCEV
 PPG
 LPFS
 LT
 SSL
 KNY
 FTL
 KTS
 ADL
 DRE
 TVPEY
 NLS
 I
 T
 AR
 DAG
 TPS
 LSALT
 IV
 RVQ
 VS
 D
 IN
 DP
 PQSS
 QSSY
 DVY
 IE
 EN
 NL
 PGAPI
 LN
 LS
 VWD
 P
 DAP
 Q
 N
 A
 RL
 S
 FF
 L
 LE
 Q
 GA
 ET
 GLV
 GRY
 FT
 IN
 RD
 NG
 IV
 SS
 LV
 PL
 DY
 ED
 R
 RE
 FEL

TAHISDGTPVLATNISVNIFVTDRNDNAPQVLYPRPGGSSVEMLPRGTSAGHLVSRVV
 GWDADAGHNAWLSYSLLGSPNQLFAIGLHTQQISTARPVQDTSRQTLTVLIKDNGE
 PSLSTTATLTVSVTEDSPEARAEFPSSGAPREQKKNLTFYLLSLILSVGFVVTFGVIIF
 KVKWKQSRLYRAPVSSLYRTPGPSLHADAVRGGLMSPHLYHQVLTTSRRSDPLL
 KKPGAAASPLASRQNTLRSCDPVFYRQVLGAESAPPGQQAPPNTDWRFSQAQRPGTS
 GSQNGDDTGTWPNNQFDTEMLQAMILASASEAADGSSTLGGGAGTMGLSARYGPQF
 TLQHVPDYZRNVYIPGSNATLTNAAGKRDGKAPAGGNGNKKSGKKEKK

SEQ ID No:59

MAAAMDVDTPSGTNSGAGKKRFEVKWNAVALWAVIDIVVDNCAICRNHIMDLCIECQA
 NQASATSEECTVAWGVCNHAFHFHCISRWLKTRQVCPLDNREWEFQKYGH

SEQ ID No:60

MDADM DYERPNVETIKCVVVGDNAGKTRLICARACNTLTQYQLLATHVPTVWAIDQY
 RVCQEVLERSRDVVDEVSVSLRLWDTFGDHDKDRRFAYGRSDVVLCFSIANPNSLNH
 VKSMWYPEIHKFCPRTPVILVGCQLDLRYADLEAVNRARRPLARPIKRGDILPPEKGREV
 AKELGLPYYETSVFDQFGIKDVFDNAIRALISRRHLQFWKSHLKKVQKPLLQAPFLPPK
 APPVVIKIECPMTNEAACLLDNPLCADVLFILQDQEHIHAFRIYLATSSSKFYDLFLM
 ECEESPNGSEGACEKEKQSRDFQGRILSVDPEEEEREGPPRIPQADQWKSSNKLVEA
 LGLEAEGAVPETQTLTGWSKGFIGMHREMQVNPIISKRMGPMTVVRMDASVQPGPFRT
 LLQFLYTGQLDEKEKDLVGLAQIAEVLEMFDLRRMMVENIMNKEAFMNQEITKAHVRA
 NRIKECLSKGTFSVTFKLDDGAISAHKPLLICSEWMAAMFGGSFVESANSEVYLPNIN
 KISMQAVLDYLYTKQLSPNLDLDPLELIALANRFCCLPHLVALAEQHAVQELTKAATSGVGI
 DGEVLSYLELAQFHNAHQLAACWCLHHICTNYNSVCSKFRKEIKSKSADNQEYFERHRW
 PPVWYLKEEDHYQRVKREREKEDIALNKHSRRKWCFWNSSPAVA

SEQ ID No:61

ACSAGR DVFLTLEATPSHVVVSRLMDSDMDYERPNVETIKCVVVGDNAGKTRLICARA
 CNATLTQYQLLATHVPTVWAIDQYRVCQEVLERSRDVVDDVSVSLRLWDTFGDHDKDR
 RFAYGRSDVVLCFSIANPNSLHHVKTMWYPEIHKFCPRAPVILVGCQLDLRYADLEAV
 NRARRPLARPIKPNEILPPEKGREVAKELGIPYYETSVVAQFGIKDVFDNAIRALISRRH
 LQFWKSHLRNVQRPLLQAPFLPPKPPPIIVVPDPPSSSEECPAHLLEDPLCADVILVLQ
 ERVRIFAHKIYLSTSSSKFYDLFLMDLSEGELEGGPSEPGGTHPEDHQGHSDQHHHHHH
 HHHGRDFLLRAASFVDCESVDEAGGSGPAGLRASTSDGILRGNGTGYLPGRGRVLSS

WSRAFVSIQEEMAEDPLTYKSRLMVVVKMDSSIQPGPFRAVLKYLYTGELDENERDLM
 HIAHIAELLEVFDLRRMMVANILNNEAFMNQEITKAHVRRNTNVKECLAKGTFSDVTFILE
 DGTISAHKPLLSSCDWMAAMFGGPVESSTREVVFVPTSKSCMRAVLEYLYTGMFTSS
 PDLDDMKLIILANRRLCLPHLVALTEQYTVTGLMEATQMMVDIDGDVLVLEAQFHCA
 QYADWCLHHICTNYNNVCRKFPRDMKAMSPENQEYFEKHRWPPWYLKEEDHYQRAR
 KEREKEDYLHLKRQPKRRLFWNSPSSPSSAASSSSPSSSAVV

SEQ ID No:62

MAAAAAMAEQESARNNGGRNRGGVQRVEGKLRAVEKGDYYEAHQMYRTLFFRYMSQ
 SKHTEARELMSGALLFFSHGQQNSAADLSMLVLESLEKAEVEVADELLENLAKVFS
 LMDPNSPERVTFSRALKWSSGGSGKLGHPRLHQQLALTWKEQNYCESRYHFLHSADG
 EGCANMLVEYSTSRGFRSEVDMFVAQAVLQFLCLKNKSSASVVFTTYTQKHPSIEDGP
 PFVEPLLNFIFWLLLAVDGGKLTVFTVLCEQYQPSLRRDPMYNEYLDRIGQLFFGVPPK
 QTSSYGGLLGNLLTSLMGSSEQEDGEESPSDGSPIELD

SEQ ID No:63

MIEPSEDASFETMMEHKNPSSKQMESSEGSSNTTEATSGSGVRGEAGPASGPAQEKK
 PPSGPLQEMEELPTDLLQDMEEPSSGPRKEIEDPPNDLLQDLEESCNGSHQARGDPLS
 GASDRMKEASVNPSGAREEQEAHTDLKESGREETPQEQNQTEHSTAELMAMVRSIISL
 YFRMQDLKEQQRVAEEILIKGINAGQLPAPKHFSGDRREFHEFIVLCQLTLQSYPRMFY
 NDRLRVGYVINHLSGLALEWAKALLQENSPLIGDFPAFLEAMSEVFEYRQALRVAEEAM
 FTIRQGGRSATEYIDEFQLVPILGWPDEVLQAHCQGLNEEIRHYLFRVPQPDSLDSI
 VLILQIEEKLAERRAMLRLLPPEARPRNLTWIDSPAPERWMVSSWLPSEVHPDINRAHLFL
 LLMVRVNPYHSVAVQALVDSGADGNFMDKEFAQEHYVELYEKPYPQPVQSVDGSLIGN
 EPVWLYTEPLVCIHQNHQESIEFDIVPSPNFSVVLGIRWLRVHAPEVDWIKGRCTFHSPY
 CLKNCFRPPPPCIALERHGMSLLPGLPHYSIDLADVFNPKEADDETSDQPSSDGSDL
 SESEPSELQQAGDSDHSETFYECPTAPWEVGARMQERARLQEEYWDLQDMLTNR
 QDYIQMIPELFQDQLHGAEWFTKLELRGTIVEESVNGHRTEDVWKAAFGLEEMKSYQP
 FALSPDPIIPQNVIFILKDMLGFFVLSYGQEVLIYSMSQEEHLHHVRQVLVRFRHHNVY
 CSLDKSQFHRQTVEFLGFVTPKGVKLNKNVMTIITGYPTPGSKLSLRNFIEFVFPYRHF
 VERFSIIAEPLVRQLLSSYQFYWGVEEQAFAECLKRAFRKAPLLHHPKPQNPFYLETGV
 TGTALHASLIQIDDQTGKRACCAFYSRNISPIEVEYSQAEMKILPIRAAFMVWCY
 LENTE EPIMILLNTEDLASLNNDRLTVLLPGHWVFFFHFNFDVME
 LPEQDGGRALPPVRNLRW RRAFQRNTAARQTLLASRGFPRDPSTESGEEENE
 EQDELNEQILRQELLAMIPIDQILN

SFLAHFSMAQIRAVILHFFRGLLYWKNTLALAAILVLLVRQCLSLRPAPAMRVARPQPQ
 RSLRLILDSSLIAGSSITTATQLLTQMPALVGANTIPAQELAELFLGPGRWQRNALHSQA
 HRGLQFTPGFWTLCEFFGVRVTPQEGLPALRQNRYLELVVGDEDVVLREALQDDL
 QRYRQCGLHDGLQDTSQDKQDNDVQEAPPSTAATHPPRPRHLMDPVLEFLGSRLL
 HIHSADGQLHLLSREQAARALSQFLTLYRRALPIPAWESQPREQARLEELPDEDEDANL
 D

SEQ ID No:64

MSDMEDDFMCDDEEDYDLEYSEDSNSEPNVDLENQYYNSKALKEDDPKAALSSFQKV
 LELEGEGEWFKALKQMIKINFKLNFPEMMNRYKQLTYIRSAVTRNYSEKSINSILD
 YISTSKQMDLLQEFYETTLEALKDAKNDRWFKNTKLGKLYEREELYGKLQKILRQLHQ
 SCQTDDGEDDLKKGTQLLEIYALEIQMYTAQKNNKKLKALYEQSLHIKSAIPHPLIMGVIR
 ECGGKMHREGEFEKAHTDFFEAFKNYDESGSPRRTTCLKYLVLANMLMKSGINPFDS
 QEAKPYKNDPEILAMTNVSAYQNNDITEFEKILKTNHSNIMDDPFIREHIEELLRNIRTQV
 LIKLIKPYTRIHIPFISKELENIDVADVESLLVQCILDNTIHGRIDQVNQNLLELDHQKRGGARY
 TALDKWTNQLNSLNQAVVSKLA

SEQ ID No:65

MATPDQKSPNVLLQNLCCRILGRSEADVAQQFQYAVRVIGSNFAPTVERDEFLVAEKIK
 KELIRQRREADAALFSELHRKLHSQGVLKKNWSILYLLLSEDPRRQPSKVSSYATLFA
 QALPRDAHSTPYYARPQTLPLSYQDRSAQSAQSSGSVGSSGISSIGLCALSGPAPAP
 QSLLPGQSNQAPGVGDCLRQQLGSRLAWTLTANQPSSQATTSGVPSAVSRNMTRS
 REGDTGGTMEITEAAALVRDILYVFQGIDGKNIKMNNTECYKVEGKANLSRSLRDTAVR
 LSELGWLHNKIRRYTDQRSLDRSFGLVGQSFCALHQELREYYRLLSVLHSQQLQLEDD
 QGVNLGLESSLTLRRLLVWTYDPKIRLKTLAALVDHCQGRKGELASAVHAYTKGDPY
 MRSLVQHILSLVSHPVLSFLYRWIYDGELEDTYHEFFVASDPTVKTDRLWHDKYTLRKS
 MIPSFMTMDQSRKVLLIGKSINFLHQVCHDQTPTKMIAVTKSAESPQDAADLFTDLENA
 FQGKIDAAYFETSKYLLDVLNKKYSLLDHMQAMRRYLLGQGDFIRHLMDDLKPELVRP
 ATTLYQHNLTGILETAVRATNAQFDSPEILRRLDVRLLEVSPGDTGWDVFSLDYHVDGPI
 ATVFTRCMSSHYLRVFNFLWRAKRMNEYILDIRKGHMCNAKLLRNMPEFSGVLHQCHIL
 ASEMVFHFIHQMQYYITFEVLECSWDELWNKVQQAQDLDHIIAAHEVFLDTIISRCLLSD
 SRALLNQLRAVFDQIELQNAQDAIYRAALEELQRRLQFEKKKQREIEGQWGVTAEE
 EENKRIGEFKESIPKMCSQLRILTHFYQGIVQQFLVLLTTSSDESLRFLSFRLDNEHYK
 AREPRLRVSLGTRGRRSSHT

SEQ ID No:66

MAVAPRLFGGLCFRFRDQNPEVAVEGRLPIHSCVGCRERTAMATVAANPAAAAAAAV
 AAAAATEDREPQHEELPGLDSQWRQIENGESGRERPLRAGESWFLVEKHWYKQWE
 AYVQGGDQDSSTFPGCINNATLFQDEINWRLKEGLVEGEDYVLLPAAWHYLVSWYGL
 EHGQPPIERKVIELPNIQKVEVYPVELLVRHNDLGKSHTVQFSHTDSIGLVLRTARERFL
 VEPQEDTRLWAKNSEGSLDRLYDTHITVLDAALETGQLIIMETRKKDGTWPSAQLHVMN
 NNMSEDEDDFKGQPGICGLTNLGNTCFMNSALQCLSNVPQLTEYFLNNCYLEELNFRN
 PLGMKGEIAEAYADLVKQAWSGHRSIVPHVFKNKVGHFASQFLGYQQHDSQELLSFL
 LDGLHEDLRVKKKEYVELCDAAGRDPQEVAQEAWQNHKRRNDSIVDTFHGLFKSTL
 VCPDCGNVSVTFDPFCYLSVPLPISHKRVLEVFFIPMDPRRKPEQHRLVVPKKGKISDLC
 VALSKHTGISPERMMVADVFSHRFYKLYQLEEPLSSILDRDDIFVYEVSGRIEAIEGSRED
 IVVPVYLERTPARDYNNSYYGLMLFGHPLLVSVPRDRFTWEGLYNVLMYRLSRYVTK
 PNSDDEDDGDEKEDDEEDKDDVPGPSTGGSLRDPEPEQAGPSSGVNRCPFLLDNCL
 GTSQWPPRRRRKQLFTLQTVNSNGTSDRTSPEEVHAQPYIAIDWEPEMKRYYDEVE
 AEGYVKHDCVGYVMKKAPVRLQECIELFTTETLEKENPWYCPCKQHQLATKKLDLW
 MLPEILIIHLKRFSYTKFSREKDTLVEFPIRDLDFSEFVIQPQNESNPELYKYDLIAVSNH
 YGGMRDGHYTTFACNKDSGQWHYFDDNSVSPVNENQIESKAAYVLFYQRQDVARRLL
 SPAGSSGAPASPACSSPPSSEFMDVN

SEQ ID No:67

MPVRKQDTQRALHLLEEYRSKLSQTEDRQLRSSIERVINIFQSNLFQALIDIQE FYEVTL
 DNPKCIDRSKPSEPIQPVNTWEISSLPSSTVSETLPSSLSPSVEKYRYQDEDTPPQEHI
 SPQITNEVIGPELVHVSEKNLSEIENVHGFVSHSHISPIKPTEAVLPSPPTVVIPVLPVPA
 ENTVILPTIPQANPPPVLVNTDSETPTYVNGTDADYEYEEITLERGNSGLGFSIAGGTD
 NPHIGDDSSIFITKIITGGAAAQDGRLRVNDCLQVNEVDVRDVTHSKAVEALKEAGSIVR
 LYVKRRKPVSEKIMEIKLIKGPKGFIAGGVGNQHIPGDNSIYVTKIIEGGAAHKDGKL
 QIGDKLLAVNNVCLEEVTHEEAVTALKNTSDFVYLKVAKPTSMYMNMDGYAPPDITNSSS
 QPVDNHVSPPSFLGQTPASPARYSPVSKAVLGDDITREPRKVVLHRGSTGLGFNIVG
 GEDGEFIGFISFILAGGPADLSGELRGDRRIISVNSVDLRAASHEQAAAALKNAGQAVTIVA
 QYRPEEYSRFEAKIHDREQMMNSSISSGSGSLRTSQKRSLYVRALFDYDGTKDGLP
 SQGLNFKFGDILHVINASDDEWWQARQVTPDGESDEVGVIPSRRVEKKERARLKTVK
 FNSKTRDKGQSFNDKRKKNLFSRKFPFYKNKDQSEQETSDADQHVTNSASDSESSYR
 GQEEYVLSYEPVNQQEVNYTRPVII LGPMKDRINDDLISEFPDKFGSCVPHTTRPKRDY

EVDGRDYHFVTSREQMEKDIQEHKFIEAGQYNNHLYGTSVQSVREVAGKGKHCILDVS
 GNAIKRLQIAQLYPISIFIKPKSMENIMEMNKRLTEEQARKTFERAMKLEQEFTEHFTAIV
 QGDTLEDIYNQVKQIEEQSGSYIWVPAKEKL

SEQ ID No:68

DLTQAKPIYGGWLLLAPDGTDFDNPVHRSRKWQRRFFILYEHGLLRYALDEMPTTLHQ
 GTINMNQCTDVVDGEGRTGQKFSLCILTPEKEHFIRAETKEIVSGWLEMLMVYPRTNKQ
 NQKKKRKVEPPTPQEPGPRAVVTSSSSSSSSIPS AKEVPTTKSTLWQEEEMRTKDQ
 PDGSSLSPAQS PQSQPPAASSLREPGLSKEEESAMSSDRMDCGRKVRVESGYFSL
 ETKQDLKAEEQQLPPPPLSPPS PTPN HRRSQVIEKFEALDIEKAEHMETNAVGPSQSS
 DTRQGRSEKRAFP RKRDFTNEAPPAPLPDASASPLSPHRRAKSLDRRSTEPSVTPDLL
 NFKKGWLT KQYEDGQWKHWFVLADQLSLYYRDSVAEEAADLDGEIDL SACYDVTEY
 PVQRNYGFQIHTKEGEFTLSAMTSGIRRNWIQTIMKHVHPTTAPDVTSSLPEEKNKSSC
 SFETCPRPTEKQEAELGEPDPEQKRSRARERRREGRSKTFDWAEFRLIQQALAQERV
 GGVGPADTHEPLRPEAEPGELERERARRREERRKRG MLDATDGP GTEDA ALRMEVD
 RSPGLPMSDLKTHNVHVEIEQRWHQVETTPLREEKQVPIAPVHLSEDGGDRLSTHEL
 TSLLEKELEQS QKEASDLLEQNRLLQDQLRVALGREQSAREGYVLQATCERGFAAMEE
 THQKKIEDLQRQHQRELEKLREEKDRLLAETTAATISAEAMKNAHREEMERELEKSQR
 SQISSVNSDVEALRRQYLEELQSVQRELEV LSEQYSQKCLENAHLAQALEAERQALRQ
 CQRENQELNAHNQELNNRLAAEITRLRTLLTG DGGGEATGSPLAQGKDAYELEVLLRV
 KESEI QYLKQEISL KDELQTA RDKKYASDKYKDIYTEL SIAKAKADC DISRLKEQLKAAT
 EALGEKSPDSATVSGYDIMKSNSNPDFLKKDRSCVTRQLRNIRSKSVIEQVSWDT

SEQ ID No:69

MAGITTIEAVKRKIQVLQQQADDAEERAERLQREVEGEK MELQE IQLKEAKHIAEEADR K
 YEEVARKLVIIEGDLERTEERAELAESRCREMDEQIRLMDQNLKCLSAAEEKYSQKEDK
 YEEEIKILTDKLKEAETRAEFAERSVAKLEKTIDDLEDKLKCTKEEHLCTQRMLDQTL LDL
 NEM

SEQ ID No:70

MACPALGLEALQPLQPEPPPPEP A FSEA QK WIEQVTGRSFGDKDFRTGLENGILLCELLN
 AIKPGLVKKINRLPTPIAGLDNIILFLRGCKELGLKESQLFDPSDLQDTSNRVTVKSLDYSR
 KLKNVLVTIYWLGAANSCTS YSGT TLNLKEFEGLLAQMRKDTDDIESPKRSIRD SGYID
 CWDSERSDSLSPPRHGRDDSFDSLDSFGSRQTPSPDVVL RGSSDGRGSDSESDL P

HRKLPDVKKDDMSARRTSHGEPKSAVPFNQYLPNKSNQTAYVAPLKKAAEREERYR
 KSWSTATSPLGGERPFRYGPRTPVSDAESTSMFDMRCEEEAAVQPHSRARQEQLQL
 INNQLREEDDKWQDDLARWKSRRRSVSQDLIKKEEERKKMEKLAGEDGTERRKSIK
 TYREIVQEKEERRERELHEAYKNARSQEEAEGILQQYIERFTISEAVLERLEMPKILERSHS
 TEPNLSSFLNDPNPMKYLQRQQSLPPPFTATVETTIARASVLDTSMSAGSGSPSKTVTP
 KAVPMLTPKPYSQPKNSQDVLKTFKVDGKVSVNGETVHREEEKERECPVTAPAHSLT
 SQMFEGVARVHGSPLELKQDNIEINIKKPNVPQELAATTEKTEPNSQEDKNDGGKS
 RKGNIELASSEPQHFTTTVTRCSPTVAFVEFPSSPQLKNDVSEEKDQKKPENEMSGKV
 ELVLSQKVVKPKSPEPEATLTFPFLDKMPEANQLHLPNLNSQVDSPSSEKSPVMTPKF
 WAWDPEEERRRQEKWQQEQRLLQERYQKEQDKLKEEWEKAQKEVEEEEERRYEE
 ERKIIEDTVVPFTVSSSSADQLSTSSSMTEGSGTMNKIDLGNQDEKQDRRWKKSFQG
 DDSDLLLKTRRESDRLEEKGSLTEGALAHSGNPVSKGVHEDHQLDTEAGAPHCGTNPQL
 AQDPSQNQQTSNPTHSSVEDVKPKTLPLDKSINHQIESPSERRKSPREHFQAGPFSPC
 SPTPPGQSPNRSISGKKLCSSCGLPLGKGAAMIIETLNLYFHIQCFRCGICKGQLGDAVS
 GTDVRIRNGLLNCNDCYMRSRSAGQPTTL

SEQ ID No:71

PLCPALCPTSPPPLPLLPPSVSPPGCLTLWSLSFLFSVPSAPYPHLTTMATIPDWKLQL
 LARRRQEAEASVRGREKAERERLSQMPAWKRGLLERRAKLGSPGEPSVLTVEAG
 PPDPDESABLSEAIGPVHQNRFIRQERQQQQQQQRSEELLAERKPGPLEARERRPSP
 GEMRDQSPKGRESREERLSPRETRERRLGIGGAQELSLRPLEARDWRQSPGEVGDRS
 SRLSEAWKWLSPGETPERSLRLAESREQSPRRKEVESRLSPGESAYQKLGLTEAHK
 WRPDSDRESQEQLVQLEATEWRLRSGEERQDYSEECGRKEEWVPGVAPKETAELS
 ETLTREAQGNSSAGVEAAEQRPVEDGERGMKPTEGWKWTLSKGAREWTPRDIEAQ
 TQKPEPPESAEKLLESPGVEAGEGEAEKEEAGAQGRPLRALQNCCSVPSPLPPEDAGT
 GGLRQQEEEAVELQPPPPAPLSPPPPAPTAPQPPGDPLMSRLFYGVKAGPGVGAPRR
 SGHTFTVNPRRSVPPATPATPTSPATVDAAVPGAGKKRYPTAEELVLGGYLRLSRSC
 AKGSPERHHKQLKISFSETALETTYQYPSESSVLEELGPEPEVPSAPNPPAAQPDDEED
 EEELLLQPELQGGLRTKALIVDESCRR

SEQ ID No:72

MTSAAPAKKPYRKAPPEHRELRLIEPGSRLEQEEPLTDAERMKLLQEENEELRRRLASA
 TRRTEALERELEIGQDCLELELGQSREELDKFKDKFRLQNSYTASQRTNQELEDKLHT
 LIKKAEMDRKTLDWEIVELTNKLLDAKNTINKLEELNERYRLDCNPNAVQLLCKNKSHFRN

HKFADLPCELQDMVRKHLHSGQEASPGPAPSLAPGAVVPTSVIARVLEKPESLLNSA
 QSGSAGRPLAEDVFVHDMSEGVPGDPASPPAPGSPTPQPNGECHSLGTARGSPEEE
 LPLPAFEKLNPYPTPSPPHPLYPGRRVIEFSEDKVRIPRNSPLPNCTYATRQAISLSLVEE
 GSERARPSPVPSTPASAQASPHHQSPAPLTL SAPASSASSEEDLLVSWQRADFDRTP
 PPAAVAQRTAFGRDALPELQRHFAHSPADRDEVVQAPSARPEESELLLPTEPDGFPR
 EEEELNLPISPPEERQSLLPINRGTEEGPGTSHTEGRAWPLPSSSRPQRSPKRMGVHH
 LHRKDSDLTQAQEQQGNLLN

SEQ ID No:73

MASTISAYKEKMKEVLICSCFYTQPHPNTVYQYGDMEVKQLDKRASGQSFEVILK
 SPSDLSPEPMISSLSSPKKKDTSLEELQKRLEAAEERRKTQEAVLKQLAERREHEREV
 LHKALEENNFSRQAEEKLNYKMELSKEIREAHLAALRERLREKELHAAEVRRNKEQRE
 EMSG

SEQ ID No:74

MAHRKLESVGSGMLDHVRVRPGPVPHSQEPESEDMELPLEGYVPEGLELAALRPESPA
 PEEQECHNHSPGDSSSDYVNNTSEEEDYDEGLPEEEEGITYYIRYCPEDDSYLEGMD
 CNGEELYLAHSAPVDTDECQEAVEEWTDASAGPHHGHEAEQSQDYPDGQLPIPEDEP
 SVLEAHDQEEDGHYCASCHEYQDYYPEEANGNTGASPYRLRRGDGDLEDQEEDIDQI
 VAEIKMSLMSMTSITSASEASPEHGPEPGPEDSVEACPPIKASCSPSRHEARPKSLNLLPE
 AKHPGDPQRGFKPKTRTPEERLKWPHEQVCNGLEQPRKQQRSDLNGPVDNNNIPETK
 KVASFPSFVAVPGCCEPEDLIDGIIFAANYLGSTQLLSERNPSKNIRMMQAQEAVSRVKR
 MQKAALKKKANSEGDAQTLTEVDLFISTQRIKVLNADTQETMMDHALRTISYIADIGNIV
 VLMARRRMPPRSASQDCIETTPGAQEGKKQYKMICHVFESEDAQLIAQSIGQAFSVAYQ
 EFLRANGINPEDLSQKEYSDIINTQEMYNDDLIHFSNSENCHELQLEKHKGELGVVVVE
 SGWGSILPTVILANMMNGGPAARSGKLSIGDQIMSINGTSLVGLPLATCQGIKGLKNQT
 QVKLNIVSCPPVTTVLIKRPDLKYQLGFSVQNGIICSLMRGGIAERGGVRVGHRIIEINGQ
 SVVATAHEKIVQALSNSVGEIHMKTPAAMFRLLTGQETPLYI

SEQ ID No:75

MQRAVPEGFGRRLGSDMGNAERAPGSRSFGPVPTLLLLAAALLAVSDALGRPSEEDE
 ELVVPELERAPGHGTTRLRLHAFDQQLDLELRPDSSFLAPGFTLQNVGRKSGSETPLPE
 TDLAHCYSGTVNGDPSSAAALSLCEGVRGAFYLLGEAYFIQPLPAASERLATAAPGEK
 PPAPLQFHLLRRNRQGDVGGTCGVVDDEPRPTGKAETEDEDEGTEGEDEGPQWSPQ

DPALQGVGQPTGTGSIRKKRFVSSHRYVETMLVADQSMAEFHGSGLKHYLLTFSVAA
 RLYKHPHSIRNSVSLVVVKILVIHDEQKGPEVTSNAALTNRNFCNWQKQHNPPSDRDAEH
 YDTAILFTRQDLCGSQTCDTLGMADVTVCDPSRSCSVIEDDGLQAAFTTAHELGHVFN
 MPHDDAKQCASLNGVNQDSHMMASMLSNLDSQPWSPCSAYMITSFLDNGHGECLM
 DKPQNPIQLPGDLPGTSYDANRQCQFTFGEDSKHCPDAASTCSTLWCTGTSGGVVLVC
 QTKHFPWADGTSCGEWKWCINGKCVNKTDRKHFDTPFHGSWMGPWGDCSRTCG
 GGVQYTMRECDNPVPKNGGKYCEGKRVRYRSCNLEDCPDNNGKTFREEQCEAHNEF
 SKASFGSGPAVEWIPKYAGVSPKDRCKLICQAKGIGYFFVLQPKVVDGTPCSPDSTSVC
 VQGQCVKAGCDRIIDSKKFDKCGVCGGNGSTCKKISGSVTSAKPGYHDIITIPTGATNI
 EVKQRNQRGSRNNGSFLAIKAADGTYILNGDYTLSTLEQDIMYGVVLRYSGSSAALERI
 RSFSPLKEPLTIQVLTGNALRPKIKYTYFVKKKESFNAIPTFSAWVIEEWGECSKSCEL
 GWQRRLVECRDINGQPASECAKEVKPASTRPCADHPCPQWQLGEWSSCSKTCGKGY
 KKRSLKCLSHDGGVLSHESCDPLKKPKHFIDFCTMAECS

SEQ ID No:76

MRLTHICCCCLLYQLGFLSNGIVSELQFAPDREEWEVVFPALWRREPVDPAGGSGGSA
 DPGWVRGVGGGSARAQAAGSSREVRSVAPVPLEEPVEGRSESRLRPPPPSEGEED
 EELESQELPRGSSGAAALSPGAPASWQPPPPPQPPPSPPPAQHAEPDGDEVLLRIPAF
 SRDLYLLLRRDGRFLAPRFAVEQRPNPGPGPTGAASAPQPPAPPDAGCFYTGAVLRHP
 GSLASFSTCGGGLMGFIQLNEDFIFIEPLNDTMAITGHPHRVYRQKRSMEEKVTEKSAL
 HSHYCGIISDKGRPRSRRKIAESGRGKRYSYKLQPQEYNIETVVVADPAMVSYHGADAARR
 FILTILNMVFNLFQHKSLGVQVNLRVIKLILLHETPPELYIGHGEKMLESFCKWQHEEFG
 KKNDIHLEMSTNWGEDMTSVDAAILITRKDFCVHKDEPCDTVGIAYLSGMCEKRKCIIA
 EDNGLNLAFTIAHEMGHNMGINHDNDHPSCADGLHIMSGEWIKGQNLGDVSWSRCSK
 EDLERFLRSKASNCLLQTNPQSVNSVMVPSKLPGMTYTADEQCQILFGPLASFCQEMQ
 HVICTGLWCKVEGEKECRTKLDPMDGTDCDLGKWCKAGECTSRTSAPEHLAGEWSL
 WSPCSRTCSAGISSRERKCPGLDSEARDCNGPRKQYRICENPPCPAGLPGFRDWQCQ
 AYSVRTSSPKHIQWQAVLDEEKPCALFCSPVGKEQPILLSEKVMMDGTSCGYQGLDICA
 NGRCQKVGCDCGGLGSLAREDHCGVCNGNGKSCKIIGDFNHTRGAGYVEVLVIPAGAR
 RIKVVEEKPAHSYLAIRDAGKQSINSWDKIEHSGAFNLAGTTVHYVRRGLWEKISAKGP
 TTAPLHLLVLLFQDQNYGLHYEYTIPLPENQSSKAPEPLFMWTHTSWEDCDATCG
 GGERKTTVSCTKIMSKNISIVDNEKCKYLTKPEPQIRKCNEQPCQTRWMWMMTEWTPCSR
 TCGKGMQSRQVACTQQLSNGTLRARERDCIGPKPASAQRCEGQDCMTVWEAGVWS
 EFSVKCGKGIRHRTVRCTNPRKKCVLSTRPREAEDCEDYSKCYVWRMGDWSKCSITC

GKGMQSRVIQCMHKITGRHGNECFSSSEKPAAYRPCHLQPCNEKINVNTITSPRLAALTF
KCLGDQWPVYCRVIREKNLCQDMRWYQRCCETCRDFYAQKLQQKS

SEQ ID No:77

MPGGPSRSPAPLLRPLLLLALAPGAPGPAPGRATEGRAALDIVHPVRVDAGGSFLS
YELWPRALRKRDVSRRDAPAFYELQYRGRELRFNLTANQHLLAPGFVSETRRRGGL
GRAHIRAHTPACHLLGEVQDPELEGGGLAAISACDGLKGVFQLSNEDYFIEPLDSAPARP
GHAQPHVYKQRQAPERLAQRGDSSAPSTCGVQVYPELESRRERWEQRQQWRRPRL
RRLHQRSVSKEKWVETLVVADAKMVEYHGQPQVESYVLTIMNMVAGLFHDPSIGNPIHI
TIVRLVLEDEEEEDLKITHHADNTLKSFKWQKSINMKGDAHPLHHDTAILLTKDLCAA
MNRPCETLGLSHVAGMCQHRSCSINEDTGLPLAFTVAHELGHSGFIQHDGSGNDCEP
VGKRPFIMSPQLLYDAAPLTWSRCSRQYITRFLDRGWGLCLDDPPAKDIIDFPSVPPGV
LYDVSHQCRLQYGAYSAFCEDMDNVCHTLWCSVGTTCHSKLDAAVDGTRCGENKWC
LSGECVPVGFRPEAVDGGWSGWSAWSICSRSCGMGVQSAERQCTQPTPKYKGRYC
VGERKRFRLCNLQACPAGRPSFRHVQCSHFDAMLYKGQLHTWVPVVNDVNPCELHC
RPANEYFAKKLRDAVVDGTPCYQVRASRDLCINGICKNVGCDFEIDSGAMEDRCGVCH
GNGSTCHTVSGTSEEAEGLGYVDVGLIPAGAREIRIQEVAEAANFLALRSEDPEKYFLN
GGWTIQWNGDYQVAGTTFTYARRGNWENLTSPGPTKEPVWIQVPASRGPGGGSRGG
VPRPSTLHGRSRPGGVSPGSVTEPGSEPGPPAAASTSVSPSLKWPNLVAAVHRGGW
GQAPLGLGGWRRHLVLMGPLPTQLFQESNPGVHYEYTIHREAGGHDEVPPPFSW
HYGPWTKCTVTCGRGEKWRHSPTCRGLVSGQGHWLQLPAHCWATTGLEVCFSEP
QFSICEMRLAIALCPRPAGRVHG

SEQ ID No:78

MAARGSGPRALRLLLLVQLVAGALRSSPARRAARRGLSEPSSIKAHEDSLLKDLFQDYE
RWVRPVEHLNDKIKIKFGGLAISQLVDVDEKNQLMTTNVWLQEWIDVKLRWNPDYGGI
KVIKVPSDSSWTPDIVLFDNADGRFEGTSTKTVIRYNGTVWTTPANYKSSCTIDVTFFP
FDLQNCSMKFGSWTYDGSQVDIILEDQDVDKRDFFDNGEWEIVSATGSKGNRTDSCC
WYPYVTYSFVIKRLPLFYTLFLIIIPCIGLSFLTFLVYLPSENGEKICLCTSVLVSLTVFLLVI
EEIIPSSSKVIPLIGEYLVFTMIFVTLSIMVTFAINIHHRSSSTHNAMAPLVRKIFLHTLPKL
LSMRSHVDRYFTQKEETESGSGPKSSRNTLEAALDSIRYITTHIMKENDVREVVEDWKFI
AQVLDRMFLWTFLVSIVGSLGLFVPVIYKWANILIPVHIGNANK

SEQ ID No:79

MEPGRRGAAALLALLCVACALRAGRAQYERYSFRSFPRDELMPLAESYRHADKYSGE
 HWAESVGYLEISLRLHRLLRDSEAFCHRNCASAPQPEPAAGLASYPELRLFGGLLRAAH
 CLKRCKQGLPAFRQSQPSREVLADFQRREPYKFLQFAYFKANNLPKAIAAAHTFLLKHP
 DDEMMLKRNMAYYKSLPGAEDYIKDLETKSYESLFIRAVRAYNGENWRTSITDMELALPD
 FFKAFYECLAACEGSREIKDFKDFYLSIADHYVEVLECKIQCEENLTPVIGGYPVEKFVAT
 MYHYLQFAYYKLNDLKNAAPCAVSYLLFDQNDKVMQQNLVYYQYHRDTWGLSDEHFQ
 PRPEAVQFFNVTTLQKELYDFAKENIMDDDEGEVVEYVDDLLEETS

SEQ ID No:80

MGKVRGLRARVHQAAVRPKGEAAPGPAPPAPPEATPPPASAAGKDWFINTNIFARTKI
 DPSALVQKLELDVRSVTSVRRGEAGSSARSVPISRGAEAKTVLPKKEKMKLRREQWL
 QKIEAIKLAEQKHREERRRRATVVVGDLHPLRDALPELLGLEAGSRRQARSRESNKPRP
 SELSRMSAAQRQQQLLEEERTRFQELLASPAYRASPLVAIGQTLARQMLEDGGQL

SEQ ID No:81

MKLPARVFFTLGSRLPCGLAPRRFFSYGTKILYQNTEALQSKFFSPLQKAMLPPNSFQG
 KVAFITGGGTGLKGMTLLSSLGAQCVIASRKMDVLKATAEQISSQTGNKVHAIQCDV
 RDPDMVQNTVSELIKVAGHPNIVINNAAGNFISPTERLSPNAWKTITDIVLNGTAFVTLEI
 GKQLIKAQKGAAFLSITTIYAETGSGFVVPSASAKAGVEAMSKSLAAEWGKYGMRFNVI
 QPGPITKGAFSRLDPTGTFEKEMIGRIPCGRLGTVEELANLAFLCSDYASWINGAVIK
 FDGGEEVLISGEFNDLRKVTKEQWDTIEELIRKTGKSG

SEQ ID No:82

MVAPGSVTSRLGSVFPFLLVLVDLQYEGAECGVNADVEKHLELGKKLLAAGQLADALS
 QFHAAVDGDPDNIAYYRRATVFLAMGKSKAALPDLTKVIQLKMDFTAARLQRGHLLLK
 QGKLDEAEDDFKKVLKSNPSENNEEKEAQSQLIKSDEMQRRLRSQALNAFGSGDYAAIAF
 LDKILEVCWDAAELRELRAECFIKEGEPRKAISDLKAASKLKNDNTEAFYKISTLYYQLGD
 HELSLSEVRECLKLDQDHKRCFAHYKQVKKLNKLIESAEELIRDGRYTDATSKYESVMK
 TEPSIAEYTVRSKERICHCFSKDEKPVEAIRVCSEVLQMEPDNVNALDRAEAYLIEEMY
 DEAIQDYETAQEHNENDQQIREGLEKAQRLLKQSQKRDYYKILGVKRNAKKQEIIKAYRK
 LALQWHPDNFQNNEEKKKAEEKFIDIAAAKEVLSDEMRKKFDDGEDPLDAESQQGGG
 GNPFHRSWNSWQGFNPSSGGPFRFKFHFN

SEQ ID No:83

MRPRKAFLLLLLGLVQLLAVAGAEGPDEDSSNRENAIEDEEEEEEDDDEEEDDLEVKEENGVLVLNDANFDNFVADKDTVLLEFYAPWCGHCKQFAPEYEKIANILKDKDPPIPVAKIDATSASVLASRFDVSGYPTIKILKKGQAVDYEGSRTQEEIVAKVREVSQPDWTPPPEVTLVLTKENFDEVVNDADIILVEFYAPWCGHCKLAAPEYEKAAKELSKRSPPiplAKVDATAETDLAKRFDVSGYPTLKIFRKGRPYDNGPREKYGIVDYMIEQSGPPSKEILTLKQVQEFLKGDDVIIIGVFKGESDPAYQQYQDAANNLREDYKFHHTFSTEIAKFLKVSQGQLVVMQPEKFQSKYEPRSHMMDVQGSTQDSAICDFVLKYALPLVGHRKVSNDAKRYTRRPLVVVYYSVDFSFDYRAATQFWRSKVLEVAKDFPEYTFIAADEEDYAGEVKDLGLSESSEDVNAAILDDESGKKFAMEPEEFDSDTLREFVTAFKKGKLKPVIKSQPVPKNNKGPVKVVVGKTFDSIVMDPKKDVLIEFYAPWCGHCKQLEPVYNSLAKKYKGQKGLVIAKMDATANDVPSDRYKVEGFPTIYFAPSGDKKNPVKFEGGDRDLEHLSKIEEHATKLSRTKEEL

SEQ ID No:84

MPEQSNDYRVVVFGAGGVGKSSLVLRVKGTFRDTYIPTIEDTYRQVISCDKSVCTLQITDTTGSHQFPAMQRRLSIKGHAFLVFSVTSKQSLEELGPIYKLIVQIKGSVEDIPVMLVGNKCDETQREVDTREAQAVAQEWKCAFMETSAKMNYNVKELFQELLTLETRRNMSLNIDGKRSGKQKRTDRVKGKCTLM

SEQ ID No:85

MHLQMREDMAKYRRMSGVRPQSFRDLETTPHWAAYDTGLELLGRQEAGLALPRLEEA LQGSLAQMESCRADCEGPEEQQGAEEEEDGAASQGGLYEAIAGHWIQLQCRQRCV GEAATRPGRSFPVPDFLPNQLRRLHEAHAQVGNLSQLAIENVLSVLLFYPEDEAAKRALN QYQAQLGEPRPGLGPREDIQRFILRSLGEKRQLYYAMEHLGTSFKDPDPWTPAALIPEA LREKLREDQEKRPWDHEPVKPKPLTYWKDVLLLEGVTLTQDSRQLNGSERAVLDGLT PAECGVLLQLAKDAAGAGARSGYRGRRSPHTPHERFEGLTVLKAQLARAGTVGSQG AKLLLEVSEVRTLTQAYFSPERPLHLSFTHLVCRSAIEGEQEQRMDLSHPVADNCVL DPDTGECWREPPAYTYRDYSGLLYLNDDFQGGDLFFTEPNALTATARVRPRCGRLVAF SSGVENPHGVAVTRGRRCALALWHTWAPEHREQEWIEAKELLQESQUEEEEEEEE MPSKDPSPPEPPSRRHQRVQDKTGRAPRVREEL

SEQ ID No:86

SLRLCPWGTHLAGPTTMRLSSLLALLRPALPLILGLSLGCSLSLLRVSWIQGEGEDPCVE AVGERGGPQNPDNRARLDQSDDEFKPRIVPYYRDPNPKYKKVLRTRYIQTELGSRERL LVAVLTSRATLSTLAVAVNRTVAHHFPRLLYFTGQRGARAPAGMQVSHGDERPAWLM

SETLRHLHTHFGADYDWFFIMQDDTYVQAPRLAALAGHLSINQDLYLGRAEEFIGAGEQ
 ARYCHGGFGYLLSRSLLLRPHLDGCRGDILSARPDEWLGRCLIDSLGVGCVSQHQG
 QQYRSFELAKNRDPEKEGSSAFLSAFAVHPVSEGTLMYRLHKRFSALELERAYSEIEQL
 QAQIRNLTVLTPEGEAGLSWPVGLPAPFTPNSRFEVLGWDYFTEQHTFSCADGAPKCP
 LQGASRADVGDALETALEQLNRRYQPRLRFKQRLLNGYRRFDPARGMEYTLDLLLEC
 VTQRGHRRALARRVSLLRPLSRVEILPMPYVTEATRQLVLPLLVAEAAAAPAFLEAFAA
 NVLEPREHALLTLLVYGPREGGRGAPDPFLGVKAAAAEERRYPGTRLAWLAVRAEA
 PSQVRLMDVSVSKKHPVDTLFFLTVTRPGPEVNRCRMNAISGWQAFFPVHFQEFPNP
 ALSPQRSPPGPPGAGPDPPSPPGADPSRGAPIGGRFDRQASAEGCFYNADYLARAR
 LAGELAGQEEEEALEGLEVMVDVFLRFSGLHLFRAVEPGLVQKFSLRDCSPRLSEELYHR
 CRLSNLEGLGGRAQLAMALFEQEQQANST

SEQ ID No:87

MGLLQLLAFLSFLALCRARVRAQEPEFSYGCAEGSCYPATGDLLIGRAQKLSVTSTCGLH
 KPEPYCIVSHLQEDKKCFICNSQDPYHETLNPDShLIENVTTFAPNRLKIWWQSENGV
 ENVTIQLDLEAEFHFTHLIMTFKTFRPAAMLIERSDFGKTWGVYRYFAYDCEASFPGIS
 TGPMKKVDDIICDSRYS DIEPSTEGEVIFRALDPFKIEDPYSPRIQNLLKITNLRIKVKLH
 TLGDNLLDSRMEIREKYYYAVYDMVVRGNFCYGHASECAPVDFNEEVEGMVHGHC
 MCRHNTKGLNCELCMDFYHDLPWRPAEGRNSNACKCNCNEHSISCHFDMAVYLATG
 NVSGGVCDQCQHNTMGRNCEQCKPFYYQHPERDIRDPNFCERCTCDPAGSQNEGIC
 DSYTDFSTGLIAGQCRCCKLNVEGEHECDVCKEGFYDLSEDGFCKSCACNPLGTIPGG
 NPCDSETGHCYCKRLVTGQHCDQCLPEHWGLSNDLDGCRPCDCDLGGALNNSCFAE
 SGQCSCRPHMIGRQCNEVEPGYYFATLDHYLYEAEEANLPGVSIVERQYIQDRIPSW
 TGAGFVRVPEGAYLEFFIDNIPYSMEYDILIRYEPQLPDHWEKAVITVQRPGRIPTSSRC
 GNTIPDDDNQVVSLSPGSRYVVLPRVCFEKGNTYTVRLELPQYTSSDSDVESPYTLID
 SLVLMPCSKSLDIFTVGSSGDGVVTNSAWETFQRYRCLENSRSVVKTPMTDVCRNIIFS
 ISALLHQTGLACECDPQGSSLSSVCDPNQGQCQCRPNVVGRTCNRCAPGTGFGGPSGC
 KPCECHLQGSVNAFCNPVTGQCHCFQGVYARQCDRCLPGHWGFPSCQPCQCNGHA
 DDCDPVTGECLNCQDYTMGHNCERCLAGYYGDPPIGSGDHCRPCPCPDGPDSGRQFA
 RSCYQDPVTLQLACVCDPGYIGSRCDDCASGYFGNPSEVGGSCQPCQCHNNIDTTDP
 EACDKETGRCLKCLYHTEGEHCQFCRGYYYGDALRQDCRKVCNYLGTQEHCGNS
 DCQCDKATGQCLCLPNVIGQNCDRCAPNTWQLASGTGCDPCNCNAHSFGPSCNEF
 TGQCQCMPGFGGRTCSECQELFWGDPDVECRACDCDPRGIETPQCDQSTGQCVCVE
 GVEGPRCDKCTRGYSGVFPDCTPCHQCFALWDVIIAELTNRTHRFLEKAKALKISGVIG

PYRETVDVERKVSEIKDILAQS PAAEPLKNIGNLFEEAEKLIKDVTEMMAQVEVKLS DTT
 SQSNSTAKELDSLQTEAESLDNTVKELAEQLEFIKNSDIRGALDSITKYFQMSLEAEERV
 NASTTEPNSTVEQSALMRDRVEDVMMERESQFKEKQEEQARLLDEAGKLQSLDLSAA
 AEMTCGTPPGASCSETECGGPNCRTDEGERKCGGPGCGGLVTVAHNAWQKAMDLD
 QDVLSALAEVEQLSKMVSEAKLRADEAKQSAEDILLKTNATKEKMDKSNEELRNLIQIR
 NFLTQDSADLDSIEAVANEVLKMEMPSTPQQLQNLTEDIRERVERVESLSQVEVILQHSAADI
 ARAEMLLEEAKRASKSATDVKVTADMVKEALEEEAKAQAEEKAQKAQADEDIQGTQNLL
 TSIESETAASEETLFNASQRISELERNVEELKRKAAQNSGEAEYIEKVVYTVKQSAEDVK
 KTLDGELDEKYKKVENLIAKKTEESADARRKAEMLQNEAKTLLAQANSKLQLLKDLERK
 YEDNQRYLEDKAQELARLEGEVRSLLKDISQKVAVYSTCL

SEQ ID No:88

MRGSHRAAPALRPRGRWLWPVLAVLAAAAAGCAQAAMDECTDEGGRPQRCMPEFVN
 AAFNVTVVATNTCGTPPEEYCVQTGVTKSCHLCDAGQPHLQHGAFLTDYNNQA
 DTTWWQSQTMLAGVQYPSSINLTLLHGKAFDITYVRLKFHTSRPESFAIYKRTREDGPW
 IPYQYYSGSCENTYSKANRGFIRTGGDEQQALCTDEFSDFSPLTGGNVAFSTLEGRPS
 AYNFDNSPVLQEWTATDIRVTLNRLNTFGDEVFNDPKVLKSYYYAISDFAVGGRCKCN
 GHASECMKNEFDKLCNCNKHNTYGVDC EKCLPFFNDRPWRRATAESASECLPCDCNG
 RSQECYFDPELYRSTGHGGHCTNCQDNTDGAHCERCRENFFRLGNNEACSSCHCSP
 VGSLSTQCDSYGRCSCKPGVMGDKDRCQPGFHSLTEAGCRPCSCDPSGSIDECSV
 ETGRCVCKDNVEGFNCERCKPGFFNLESSNPRGCTPCFCFGHSSVCTNAVGSVYSIS
 STFQIDEDGWRAEQRDGSEASLEWSSERQDIAVISDSYFPRYFIAPAKFLGKQVLSYQQ
 NLSFSFRVDRRDTRLSAEDLVLEGAGLRVSPLIAQGNSYPSETTVKYVFRHLHEATDYP
 WRPALTPFEFKLLNNLTSIKIRGTYSERSAGYLDDVTLASARPGPGVPATWVESCTCP
 VGYGGQFCMCLSGYRRETPNLGPYSPCVLCACNGHSETCDPETGVCNCRDNTAGP
 HCEKCS DGYYGDSTAGTSSDCQPCPCPGGSSCAVVPKTKEVVCTNCPTGTTGKRC
 CDDGYFGDPLGRNGPVRLCRLCQCSDNIDPNAVGNCNRLTGECLKCIYNTAGFYCDR
 CKDGFFGNPLAPNPADKCKACNCNPYGTMKQQSSCNPVTGQCECLPHVTGQDCGAC
 DPGFYNLQSGQGCERCDCHALGSTNGQCDIRTGQCECQPGITGQHCEVNHFGF
 GPEGCKPCDCHPEGSLSLQCKDDGRCECREGFVGNRCQCEENYFYNRSWPGCQE
 CPACYRLVKDKVADHRVKLQELESLIANLGTGDEMVTQAFEDRLKEAEREVMDLLRE
 AQDVKDQNLMDRLQRVNNTLSSQISRLQNI RNTIEETGNLAEQARAHVENTERLIEIA
 SRELEKAKVAAANVSVTQPESTGDPNNMTLLAEEARKLAERHKQEADDIVRVAKTAND
 TSTEAYNLLRTLGENQTA FIEELNRKYEQAKNISQDLEKQAARVHEEAKRAGDKAV

EIYASVAQLSPLDSETLENEANNIKMEAENLEQLIDQKLKYEDLREDMRGKELEVKNLL
 EKGKTEQQTADQLLARADAALKALAEAAKKGRDTLQEANDILNNLKDFDRRVNDNKTA
 AEEALRKIPAINQTITEANEKTREAQQALGSAAADATEAKNKAHEAERIASAVQKNATST
 KAEAERTFAEVTDLDNEVNNMLKQLQEAEKELKRKQDDADQDMMMAGMASQAAQEA
 EINARKAKNSVTSLISIINDLLEQLGQLDTVDLNLNEIEGLNKADEMVKSDLDRKVSD
 LENEAKKQEEAIMDYNRDIEEIMDIRNLEDIRKTLPSGFNTPSIEKP

SEQ ID No:89

MRRAPCVRDKLREIVGASTNWRDHVKAMEERKLLHSFLAKSQDGLPPRRMKDSYIEVL
 LPLGSEPELREKYLTVQNTVRFGRILEDLSLGVLYCIMHNKIHSAKMSPLSIVTALVDKI
 DMCKKSLSPEQDIKFSGHVSWVGKTSMEVKMQMFQLHGDEFCPVLDATFVMVARDSE
 NKGPAFVNPLIPESPEEEELFRQGELNKGRRIAFSSTSLLKMAPSAEERTTIHEMFLSTL
 DPKTISFRSRVLPSNAWMENSKLKSLEICHPQERNIFNRIFGGFLMRKAYELAWATAC
 SFGGSRPFVVAVDDIMFQKPVEVGSSLFLSSQVCFTQNNYIQVRVHSEVASLQEKGHTT
 TNVFHFTFMSEKEVPLVFPKTYGESMLYLDGQRHFNSMSGPATLRKDYLVEP

SEQ ID No:90

MRGSQEVLMWLLVAVGGTEHAYRPGRRVCAVRAHGDVSESFVQRVYQPFLTTCD
 GHRACSTYRTIYRTAYRRSPGLAPARPRYACCPGWKRTSGLPGACGAAICQPPCRNG
 GSCVQPGRCRCPAGWRGDTQCSDVDECSARRGGCPQRCVNTAGSYWCQCWEGH
 LSADGTLCPKGPPRVPAPNPTGVDSAMKEEVQRLQSRVLLEEKLQLVLAPLHSLAS
 QALEHGLPDPGSLLVHSFQQLGRIDSLSEQISFLEEQLGSCSKKDS

SEQ ID No:91

MTLARFVLALMLGALPEVVGFDSDLNDSLHHSHRHSPAGPHYPYLYPTQQRPPTRP
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 VPPFLERSPPASWAQLRGQRHNFCRSPDGAGRWPWFYGDARGKVDWGYCDCRHGS
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 LGЛИPIYWSNVRCRGDEENILLCEKDIWQGGVCPQKMAAAVTCFSHGPTFIIRLAGGS
 SVHEGRVELYHAGQWGTVCDDQWDDADAECVICRQLGLSGIAKAWHQAYFGEGLGPV
 MLDEVRCTGNELSIEQCPKSSWGEHNCGHKEDAGVSCTPLTDGVIRLAGGKGSHEGR
 LEVYYRGQWGTVCDDGWTELNTYVVCRLQLGFYKGKQASANHFEESTGPIWLDDVSCS
 GKETRFLQCSRRQWGRHDCSHREDVSIACYPGGEGHRLSLGFPVRLMDGENKKEGR
 VEVFINGQWGTICDDGWTDKDAAVICRQLGYKGPARARTMAYFGEKGPIHVDNVKCT

GNERSLADCIKQDIGHNCRHSEDAVGICDYFGKKASGNSNKESLSSVCGLRLHRRQ
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 SYAVRVGVDYHTLVPEEEFEEIGVQQIVIHYREYRPDRSDYDIALVRLQGPEEQCARFSSH
 VLPACPLWRERPQKTASNCYITGWGDTGRAYSRTLQQAAIPLPKRFCEERYKGRFT
 GRMLCAGNLHEHKRVDSCQGDSGGPLMCERPGESVVYGVTSWGYGCGVKDSPGV
 YTKVSAFVPWIKSVTKL

SEQ ID No:92

MQKELGIVPSCPGMKSPRPHLLLPLLLLLLGGAGVPGAWGQAGSLDLQIDEEQPAGT
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 VTPDGATVEVTVRVADINDHAPAFPQARAALQVPEHTAFGTRYPLEPARADAGRLGT
 QGYALSGDGAGETFRLETRPGPDGTPVPELVVTGELDRENRSHYMLQLEAYDGGSPP
 RRAQALLDVTLIDINDHAPAFNQSRYHAVVSESAPGSPVLQVFASDADAGVNGAVTY
 EINRRQSEGDPFSIDAHTGLLQLERPLDFEQRRVHELVVQARDGGAHPELGSAFVTV
 HVRDANDNQPSMTVIFLSADGSPQVSEAAPPQLVARISVSDPDDGDFAHVNVSLEGG
 EGHFALSTQDSVIYLCVARRLDREERDAYNLRTATDSGSPPLRAEAAFVLHVTDVND
 NAPAFDRQLYRPEPLPEVALPGSFVVRTARDPDQGTNGQVTYSLAPGAHTHWFSIDP
 TSGIITTAASLDYELEPQPQLIVVATDGGLPPLASSATVVALQDVNDNEPQFQRTFYNA
 SLPEGTQPGTCFLQVTADSGPFGILLSYSLGAGLGSSGSPPFRIDAHSVDCTTRTL
 DRDQGPSSFDFTVAVDGGGLKSMVYVKVFLSDENDNPPQFYPREYAASISAQSPPGT
 AVLRLRAHDPDQGSHGRLSYHILAGNSPPLFTLDEQSGLLTVAWPLARRANSVQLEIG
 AEDGGGLQAEPSARVDISIVPGTPTPPIFEQLQYVFSVPEDVAPGTSVGIVQAHNPPGR
 LAPVTLSLSGGDPRGLFSLDAVSGLLQTLRPLDRELLGPVLELEVRAAGSGVPPAFVAR
 VRVLLDDVNDNSPAFPAPEDTVLLPPNTAPGTPYTLRALDPDSGVNSRVTFTLLAGGG
 GAFTVDPTTGHVRLMRPLGPSGGPAHELELEARDGGSPRTSHFRLRVVQDVGTRG
 LAPRFNSPTYRVDLPGSTTAGTQVLQVQAQAPDGGPITYHLAAEGASSPFGLEPQSGW
 LWVRAALDREAQELYILKVMAVSGSKAELGQQGTATVRVSILNQNEHSPRLSEDPTFL
 AVAENQPPGTSVGRVFATDRDSGPNGLTYSLQQLSEDSKAFRIPHQTGEVTTLQTL
 REQQSSYQLVQVQDGGSPRSTTGTVHVAVLDLNDNSPTFLQASGAAGGGLPIQVPD
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 GSLLGSVAAPEPAGVGALTYTLVGGADPEGTFALDAASGRYLARPLDFEAGPPWRAL
 TVRAEGPGGAGARLLRVQVQVQDENEHAPAFARDPLALPENPEPGAALYTFRASDA
 DGPGPNSDVRYRLLRQEPPVPALRLDARTGALSAPRGLDRETTPALLLVEATDRPANA

SRRRAARVSARVFVTDENDNAPVFAASPSRVRLPEDQPPGPAALHVVARDPDLGEAAR
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SVADVNDÉAPTFQQQEYSVLLRENNPPGTSLTLRATDPDVGANGQVTYGGVSSESFS
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EKGTFSIQPSTGAITVRSAGLDFEVSPRLRLVQAESGGAFATVLTTLQDANDNAPR
FLRPHYVAFLPESRPLEGPLLQVEADDLDQGSGGQISYSLAASQPARGLFHVDPTTGTI
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LLGSEIAQVTGNDVDSGPVLWYVLSGPQDPFSVGRYGRVSLTGPLDFEQCDRYQ
LQLLAHDGPHEGRANLTVLVEDVNDNAPAFSQSLYQVMLEHTPPGSAILSVSATDRDS
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ARATVHVQLQDQNDHAPSFTLSHYRVAVTEDLPPGSTLLTLEATDADGSRSHAAVDYSI
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PQSSVVPVTVLDVNDNPPVTRASYRVTPEDTPVGAELLHVEASDADPGPHGLVR
FTVSSGDPGLFELDESSGTLRLAHALDCETQARHQLVVQAADPAGAHFALAPVTIEVQ
DVNDHGPAPLNLSTSVAENQPPGTLVTLHAIDGDAGAFGRLRYSLLAEGPGPEGRE
AFALNSSTGELRARVPFDYEHTESFRLLVGAADAGNLSASVTVSLVTGEDEYDPVFLA
PAFHfqVPEGARRGHSLGHVQATDEDGGADGLVLYSLATSSPYFGINQTTGALYLRVD
SRAPSGTATSGGGGRTRREAPRELRLLEVIARGPLPGSRSATPVTVDITHALGLAPD
LNLLLVGAVAASLGVVVLALAALVGLVRARSRKAEAAPGPMSSQAAPLASDSLQKLGR
EPPSPPPSEHLYHQTLPSYGGPGAGGPYPRGGSLDPHSSGRGSAEAAEDDEIRMINE
FPRVASVASSLAARGPDSGIQQDADGLSDTSCEPPAPDTWYKGRKAGLLPGAGATLY
REEGPPATATAFLGGCGLSPAFTGDYGFADGKPCVAGALTAIVAGEEEELRGSYNWDY
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MRPLLLLALLGWLLLAEAKGDAKPEDNLLVLTATKETEGFRRFKRSAQFFNYKIQALGL
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 PTPFVSLFFQRLLRLHYPQKHMRLFIHNHEQHHKAQVEEFLAQHGSEYQSVKLGVPEV
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 RLWSNFWGALSADGYYARSEDYDIVQGRRVGWWNVPYISNIYLIKGSALRGELQSSD
 LFHHSKLDPDMAFCANIRQQDVFMFLTNRHTLGHLLSLDSYRTTHLHNDLWEVFSNPE
 DWKEKYIHQNYTKALAGKLVETPCPDVYWFPIFTEVACDELVEEMEHFGQWSLGNNKD
 NRIQGGYENVPTIDIHMNQIGFEREWHKFLLEYIAPMTEKLYPGYYTRAQFDLAFVRYK
 PDEQPSLMPHHDASTFTINIALNRGVVDYEGGGCRFLRYNCISRAPRKWGTLMPGRL
 THYHEGLPTTRGTRYIAVSFVDP

SEQ ID No:94

MTSSGPGPRFLLLPLLPAAASASDRPRGRDPVNPEKLLVITVATAETEGYLRFRLRSAE
 FFNYTVRTLGLGEWRGGDVARTVGGGQKVWLKEMEKYADREDMIIMFVDSYDVIL
 AGSPTELLKKFVQSGSRLLFSAESFCWPEWGLAEQYPEVGTGKRFLNSGGFIGFATTIH
 QIVRQWKYKDDDDDDQLFYTRLYLDPLREKLSLNLDHKSRIFQNLngALDEVVLKFDRN
 RVRIRNVAYDTLPIVHGNGPTKLQLNYLGNYVPNGWTPEGCGFCNQDRRTLPGGQ
 PPPRVFLAVFVEQPTPFLPRFLQRLLLLDYPPDRVTLFLHNNEVFHEPHIADSWPQLQD
 HFSAVKLVGPEEALSPGEARDMAMDLCRQDPECEFYSLSLDAVLTNLQTLRILIEENR
 KVIAPMLSRHGKLWSNFWGALSPDEYYARSEDYVELVQRKRVGVWNVPYISQAYVIRG
 DTLRMELPQRDVFSGSDTDPMADFCKSFRDKGIFLHLSNQHEFGRLLATSRYDTEHLH
 PDLWQIFDNPVDWKEQYIHENSRALEGEGEGIVEQPCPDVYWFPLLSEQMCDELVAE
 HYGQWSSGRHEDSRLAGGYENVPTVDIHMKQVGYEDQWLQLLRTYVGPMTESLFPG
 YHTKARAVMNFVVRYPDEQPSLRPHDSSTFLNVALNHKGLDYEGGGCRFLRYDC
 VISSPRKGWALLHPGRLTHYHEGLPTTWGTRYIMVSFVDP

SEQ ID No:95

MAACTARRPLAVGSRWWRSRSLTGARWPKPLCAAAGAGAFSPASTTTRRHLSSRNRP
 EGKVLETGVFEVPKQNGKYETGQLFLHSIFGYRGVVLFPWQARLYDRDVASAAPEKA
 ENPAGHGSKEVKGKHTYYQVLIDARDCPHISQRSQTEAVTFLANHDDSRALYAIPGLD
 YVSHEDILPYTSTDQVPIQHELPFERFLYDQTKAPPVARETLRAWQEKNHPWLELSDV

HRETTEINIRVTVIPFYMGMR EAQN SHVYWWRYCIRLENL DSDVVQLRERHWRIFSLSG
 TLETVRGRGVVGREPVL SKEQPAFQYSSH VSLQASSGHMWGTFRFERPDGSHFDVRI
 PPF SLESNKDEKTPPSGLHW

SEQ ID No:96

METIWIYQFRLIVIGDSTVGKCLLHRFTQGRFPGLRSPACDPTVGVDFFSRLLEIEPGK
 RIKLQLWDTAGQERFRSITRSYYRNSVGGFLVFDITNRRSFEHVKD WLEEAKMYVQPF
 RIVFLLVGHKCDLASQRQVTREEAEKLSADCGMKYIETS AKA DATNVEESFTILTRDIYELI
 KKGEICIQDGWEGVKSGFVPNTVHSSEEAVKPRKECFC

SEQ ID No:97

MERSGWARQTFL ALLLGATLRARA AAGYYPRFSPFFF LCTHGELEGDGEQGEVLISL
 HIAGNPTYVPGQEYHTISTSTFFDGLLVTGLYTSTS VQASQSIGGSSAFGFGIMSDHQ
 FGNQFMCSVVASHVSHLPTTNLSFIWIAPPAGTGCVNFMATATHRGQVIFKD ALAQQLC
 EQGAPTDVTVPHLAEIHSDSIILRDDFDSYHQLQLNPNIWECNNCETGEQCGAIMHG
 NAVTFCEPYGPRELITTGLNTTASVLQFSIGSGSCRFSYSDPSIIVLYAKNNSADWIQLE
 KIRAPS NVSTIIHILYLPEDA KGENVQFWKQENLRVGEVYEACWALDNILIINS AHRQVV
 LEDSLDPVDTGNWLFFPGATVKHSCQSDGNSIYFH GNEGSEFNFA TRDVLSTEDIQ
 EQWSEEFESQPTGWDV LGAVIGTECGTIESGLSMVFLKDGERKLCTPSMDTTGYGNLR
 FYFVMGGICDPGN SHENDIILYAKIEGRKEHITLDL TSYSSYKVPSLVS VVINPELQTPATK
 FCLRQKNHQGHNRNVWADFFHVLVLPVLPSTM SHMIQFSINLGCGTHQPGNSVSLEFST
 NHGRSW SLLHTECLPEICAGPHLPHSTVYSS ENYSGWNRITIPLPNA ALTRNTRIRWRQ
 TGPILGNMWAIDNVYIGPSCLKFCSGRGQCTR HGCKCDPGFSGPACEMASQTFPMFIS
 ESFGSSRLSSYHN FYSIRGAEVSGCGVL ASGKALV FNKEGRRQLITSFLDSSQSRFLQ
 FTLRLGSKSVL STCRAPDQPGEGVLLHYSYDNGITWLLEHYSYLSYHEPRIISVELPGD
 AKQFGIQFRWWQPYHSSQREDVWAIDEIIMTSVLFNSISLDFTNLVEVTQSLGFY LGNV
 QPYCGHDW TLCFTGDSKLASSMRYVETQSMQIGASYMIQFSLVMCGQKYTPHMDN
 QVKLEYSTNHGLTWHLVQEECLPSMPSCQEFTSASIYHASEFTQWRRVIVLLPQKTWS
 SATRFRWSQSYYTAQDEWALDSIYIGQQCPNMCS GHGSCDHGICRC DQGYQGTECH
 PEAALPSTIMSDFENQNGWESDWQEVIGGEIVKPEQCGVISSGSSLYFSKAGKRQLV
 SWDLDT SWDFVQFYI QIGGESASC NKPD SREEGVLLQYSNNGGIQWHLLAEMYFSDF
 SKPRFVYLELPAAAKTPCTRFRWWQPVFSGEDYDQWA VDDIIILSEKQKQIIPVINPTLP
 QNFYEKPAFDYP MNQMSVWLMLANE GMVKNETFC AATPSAMIFGKSDGDRFAVTRDL
 TLKPGYVLQFKLNIGCANQFSSTAPVLLQYSHAGMSWFLVKEGCY PASAGKGCEGNS

RELSEPTMYHTGDFEEWTRITIVPRSLASSKTRFRWIQESSSQKNVPPFGLDGVYISEP
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 QVGTGCGTLNDGKSLYFNGPGKREARTVPLDTRNIRLVQFYIQIGSKTSGITCIKPRTRN
 EGLIVQYSNDNGILWHLLRELDMSFLEPQIISIDLPQDAKTPATAFRWWQPQHGKHSA
 QWALDDVLIGMNDSSQTGFQDKFDGSIDLQANWYRIQGGQVDIDCLSMDTALIFTENIG
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 VRDCLPTNVECSRYHLQRILVSDTFNKWTRITLPLPPYTRSQATRFRWHQPAFKDQQ
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 PSSQNWLTVNGGKLSTVCGAVASGMALHFSGGCSRLLTVDLNLNAEFIQFYFMYGC
 LITPNRNQGVILLEYSVNGGITWNLLMEIFYDQYSKPGFVNILLPPDAKEIATRFRWWQP
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 EDKTSVNEHWLFHDDCTVERFCDSPDGVMLCGSHDGREVYAVTHDLPTEGWIMQFK
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 PGYSGPNCYLTHFLKERFDSEEIKPDLWMSLEGGSTCTECGILAEDTALYFGGST
 VRQAVTQDLDLRLGAKFLQYWGRIGSENNMTSCHRPICRKEGVLLDYSTDGGITWTLLH
 EMDYQKYISVRHDYILLPEDALTNTTRLRWQPFVISNGIVVSGVERAQWALDNILIGGA
 EINPSQLVDTFDDEGTSHHEENWSFYPNAVRTAGFCGNPSFHLYWPNNKKDKTHNALSS
 RELIIQPGYMMQFKIVVGCEATSCGDLHSVMLEYTKDARSDSWQLVQTQCLPSSNSIG
 CSPFQFHEATIYNSVNSSWKRTIQLPDHVSSSATQFRWIQKGEETEKQSWAIDHVYIG
 EACPKLCSGHGYCTTGAICIDESFQGDDCSVFSHDLPSYIKDNFESARVTEANWETIQ
 GGVIGSGCGQLAPYAHGDSLYFNGCQIRQAATKPLDLTRASKIMFVLQIGSMSQTDSCN

SDLSGPHAVDKAVLLQYSVNNGITWHVIAQHQPKDFTQAQRVSYNVPLEARMKGVLLR
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 P

SEQ ID No:98

MARVAWGLLWLLGSAGAQYEKYSFRGFPPEDLMPLAAAYGHALEQYEGESWRESARYLEAALRLHRLLRDSEAFCHANCSGPAPAAKPDPDGGRADEWACELRLFGRVLERAACLRRCKRTLPQVPPRQLLDFQSRLPYQYLHYALFKANRLEKAVAAAYTFLQRNPKHELTAKYLNYYQGMLDVADESLTDLEAQPYEAVFLRAVKLYNSGDFRSSTEDMERALS EYLAVFARCLAGCEGAHEQVDFKDFYPAIADLFAESLQCKVDCEANLTPNVGGYFVDKF VATMYHYLQFAYYKLNDVRQAARSAASYMLFDPKDSVMQQNLVYYRFHRARWGLEEE DFQPREEAMLYHNQTAELRELLEFTHMYLQSDDEMELEETEPPEPEDALSDAEFEGE GDYEEGMYADWWQEPDAKGDEAEAEPEPELA

SEQ ID No:99

MQSRLLLLGAAPGGLGDVASRRVRLLRQVLRGPGGDQQRLEVRLHSGATDSGETV SIGDVSYKLKTPKNPELVPQNYISDSPAQSIVQHLRWLMQKDLLGQDVFLIGPPGPLRR SVAMQYLELTKREVEYIALSRDTTETDLKQRREIRAGTAFYIDQCAVRAATEGRTLVLEG LEKAERNVLPVLNNLLENREMQUEDGRFLMSAERYDKLLQDHTKEELDAWKIVRVSEN FRVIALGLPVPRYSGNPLDPLRSRFQARDIYFLPFQDQLKLLYSGANVSAEKISQLLS FATTLCSQESSTLGLPDFPLDSLPEAVQILDSFPMMSIEHALQWVYPYTLLGHEGKMA VEGVLKRFEIQSGSGHSLLPKEIVRVERMTDSHGSYAHVTIRAGKEVTIKVPAGTRAVN QPCAPDHFIQTVSHKQLLAEMVQSHMVKDICLIGGKGCGKTVIAKNFAALLGYSIEPIML YQDMTARDLLQQRYTLPNGDTAWRSSPLVSAAREGKLVLDGIHRVNAGTLAVLQRLIH DRELSLYDGSRLLREDRYLSLKERLQLTDEQLQNRSIFPIHPSFRIIALAEPPIVGSTTQQ WLGPEFLTMFFFHHMKPLVKSEEIQVIKETVPNVPQEALEKLLSVTHKLRETQDPTAQSL AASLSTRQLLRISRRLSKYPSENLHDAITKACLSRFLPSLAQSALEKNLADAIIETNTEDS LEPELENYKCKVVAGSLKIGAVSVPVHNAHEKMKVPDVLFYDNVQHMVVMEDMLKDFV LGEHLLLVGNQGVVGKNKIVDRFLHLLNRPREYIQLHRDTTVQSLTLQPTVKGGLIVYEDS PLVKAVKLGHILVVDEADKAPTNTVTCILKTLVENGEAMILADGRRIVADAANVDGRENLIAI HPDFRMLALANRPGFPFLGNDFFGTLGDIIFSCHAIDNPKPHSELMLKQYGPDVPEPVL QKLVAAFGELRNLADQGIINYPYSTREVNNIVKHLQKFPTEGLSSVVRNVFDfdsynnd MREILMNTLHKYGIPIGAKPTNVQLAKE

SEQ ID No:100

MNLILEFLLLGVVIYSYLESVKFFIPRRRKSVTGQTVLITGAGHGIGRLTAYEFAKQKSR
 LVLWDINKRGVEETADKCRKLGAVVHFVVDCSNRAEIYNSVDQVKREVGDVEIVVNA
 GAIYPADLLSAKDEEITKTFEVNILGHFWIIKALLPSMLRRNSGHIVTVASVCGHGVIPYLIP
 YCSSKFAAVGFHRALTAELDTLGKTGIKTSCLCPVFVNTGFTKNPSTRLWPVLEPEEVA
 RSLINGILTNKKMIFVPSYINIFLILEKGPGFSSKPHGGSQQPVTPIPGDLTPSSDFLK
 H

SEQ ID No:101

MNTSQVEALGIQMLPGYRDPYHGRPLTKGELGCFLSHYNIWKEVVDRGPQKSLVFEDD
 LRFEIFFKRRLMNLMRDVEREGLDWDLIYVGRKRMQVEHPEKAVPRVRNLVEADYSYW
 TLAYVISLQGARKLLAAEPLSKMLPVDEFLPVMFDKHPVSEYKAHFSLRNLHAFSVEPLLI
 YPTHYTGDDGYVSDTETSVWWNNEHVKTDWDRAKSQKMREQQALSREAKNSDVLQS
 PLDSAARDEL

SEQ ID No:102

MAPAKATNVVRLLLGSTALWLSQLGSGTVAASKSVTAHLAAKWPETPLLLEASEFMAEE
 SNEKFWFQFLETVQELAIYKQTESDYSYYNLILKKAGQFLDNLHINLLKFAFSIRAYSPAIQ
 MFQQIAADEPPPDGCNAFVVIHKKHTCKINEIKKLLKKAASRTRPYLFKGDHKFPTNKEN
 LPVVILYAEMGTRTFSAFHKVLSEKAQNEEILYVLRHYIQKPSSRKMYLSGYGVELAIKST
 EYKALDDTQVKVTNTTVEDETETNEVQGFLFGKLKEIYSDLRDNLTAFKYLIIESNKQM
 MPLKVWELQDLSFQAASQIMSTPVYDAIKLMKDISQNFPPIKARSLTRIAVNQHMREEIKE
 NQKDLQVRFKIQPGDARLFINGLRVDMDVYDAFSILDMLKLEGKMMNGLRNLGINGED
 MSKFLKLN SHIWEYTYVLDIRHSSIMWINDLENDLYITWPTSCQKLLKPVFPGSVPSIRR
 NFHNLVLFIDPAQEYTLDFIKLADVFYSHEVPLRIGFVFIINTDDEVDGANDAGVALWRAF
 NYIAEEFDISEAFISIVHMYQKVKKDQNILTVDNVKSVLQNTFPHANIWDILGIHSKYDEER
 KAGASFYKMTGLGPLPQALYNGEPFKHEEMNIKELKMAVLQRMMMDASVYLQREVFLGT
 LNDRTNAIDFLMDRNNVVPRINTLILRTNQQYLNLISTSVTADVEDFSTFFFQDSQDKSAV
 IAKNMYYLTDDESIISAVTLWIIADFDKPSGRKLLFNALKHMKTSVHSRLGIYNPTSKIN
 EENTAISRGILAFLTQKNMFLRSFLGQLAKEIATTIYSGDKIKTFLIEGMKDKNafeKKYN
 TVGVNIFRTHQLFCQDVLRPGEMGIVSNGRFLGPLDEDFYAEDFYLLEKITFSNLGEK
 IKGIVENMGINANNMSDFIMKVDALMSSVPKRASRYDVTFLRENHSVIKTNPQENDMFF
 NVIAIVDPLTREAQKMAQLLVLGKIINLKIKLFMNCRGRRLSEAPLESFYRFVLEPELMSG
 ANDVSSLGPVAKFLDI PESPLLI LNMITPEGWL VETVHSNC LDNIHLKDTEKTVTAEYEL
 EYLLLEGQCFDKVTEQPPRGLQFTLGTKNKPAVVDTIVMAHHGYFQLKANPGAWILRLH

QGKSEDIYQIVGHEGTDSQADLEDIIVVLSFKSKILVKVKKETDKIKEDILTD EDEKTKG
 LWDSIKSFTVSLHKENKKEKDVLNIFSVASGHLYERFLRIMMLSVLRNTKTPVKFWLLKN
 YLSPTFKEVIPHMAKEYGFRYELVQYRWPRLQQTERQRIIWGYKILFLDVLFPLAVD
 KIIFVDADQIVRHDLKELRDFDLDGAPYGYPFCDSRREMDGYRFWKTGYWASHLLRR
 KYHISALYVVVDLKKFRRIGAGDRLRSQYQALSQDPNSLSNLDQDLPNNMIYQVAIKSLPQ
 DWLWCETWCDDESKQRAKTIDLCNNPKTKESKLKAAARIVPEWVEYDAEIRQLLDHLE
 NKKQDTILTDEL

SEQ ID No:103

MADKVRRQRPRRRVCVALVAVLLADLLASDTAVMSVDLGSESMKVAIVKPGVPMEI
 VLNKESRRKTPVITLKENERFFGDSAASMAIKNPATLRYFQHLLGKQADNPHVALYQ
 ARFPEHELTFDPQRQTVFQISSQLQFSPEEVLMVNLNSRSLAEDFAEQPIKDAVITVP
 VFFNQAERRAVLQAARMAGLKVQLINDNTATALSYGVFRKDINTTAQNIMFYDMGSG
 STVCTIVTYQMVKTEAGMQPQLQIRGVGFDRTLGGLEMELRLRERLAGLFNEQRKGQ
 RAKDVRENPRAMAKLLREANRLKTVLSANADHMAQIEGLMDDVDFKAKVTRVEFEELC
 ADLFERVPGPVQQALQSAEMSLDEIEQVILVGGATRVPRVQEVLKAVGKEELGKNINA
 DEAAAAMGAVYQAAALSKAFVKVPFVVRDAVYPILVFTREVEEEPGIHSLKHNKRVLF
 SRMGPYPQRKVITFNRYSHDFNFHINYGDLGFLGPEDLRVFGSQNLTTVKLKGVGDSF
 KKYPDYESKGIAHFNLDESGVLSLDRVESVFETLVEDSAEEESTLTKLGNTISSLFGGG
 TTPDAKENGTDVQEEEESPAEGSKDEPGEQVELKEEAEAPVEDGSQPPPPEPKGDA
 TPEGEKATEKENGDKSEAQKPSEKAEGPEGVAPAPEGEEKQKPKARKRRMVEEIGVEL
 VVLDLPDLPEDKLAQSVQKLQDLTLRDLEKQEREKAANSLEAFIFETQDKLYQPEYQEV
 STEEQREEISGKLSAATWLEDEGVGATTVMLKEKLAELRKLCQGLFFRVEERKKWPE
 RLSALDNLLNHSSMFLKGARLIPEMDQIFTEVEMTLEKVINETWAWNATLAEQAKLPA
 TEKPVLLSKDIEAKMMALDREVQYLLNKAKFTKPRPRPKDKNGTRAEPPLNASASDQG
 EKVIPPAGQTEDAEPISEPEKVTGSEPGDTEPLELGGPGAEPEQKEQSTGQKRPLKN
 DEL

SEQ ID No:104

LVRLPDGGGRRLVSQAVHGGENRGGLGCVRAIQCLVPSYSPRPRSSMFTRAQV
 RRILQRVPGKQRFGIYRFLPFFFVLGGTMEWIMIKVRVGQETFYDVRRKASERQYQRR
 LEDE

SEQ ID No:105

MSNGYEDHMAEDCRGDIGRTNLIVNYLPQNMTQDELRSLFSSIGEVESAKLIRDKVAGH
 SLGYGFVNVTAKDAERAINTLNGLRLQSKTIVSYARPSSEVIKDANLYISGLPRTMTQ
 KDVEDMFSRFGRIINSRVLDQTTGLSRGVAFIRFDKRSEAEAAITSFNGHKPPGSSEPI
 TVKFAANPNQNKNVALLSQLYHSPARRFGGPVHHQAQRFRFSPMGVDHMSGLVNV
 PGNASSGWCIFIYNLGQDAEGLWQMFGPFGAVTNVKVIRDFNTNKCKGFGVTMTN
 YEEAAMAIASLNGYRLGDKILQVSFKTNKSHK

SEQ ID No:106

MRDRLPDLTACRKNDDGDTVVVEKDHFMDFFHQVEEIRNSIDKITQYVEEVKKNHSII
 LSAPNPEGKIKEELEDLNKEIKKTANKIAAKLKAIEQSFDDQDESGNRTSVDLRIRRQHSV
 LSRKFVEAMAEMYNEAQTLFRERSKGRIQRQLEITGRTTDDELEEMLESGKPSIFTSIDIIS
 DSQITRQALNEIESRHKDIMKLETSIRELHEMFMDMAMFVETQGEMINNIERNVMNATD
 YVEHAKEETKKAIKYQSKARRKKWIIIAVSVVLVVIIVLIIGLSVGK

SEQ ID No:107

MYREWVVNVFMMLYVQLVQGSSNEHGPVKRSSQSTLERSEQQIRAASSLEELLRITH
 SEDWKLWRCRLRLKSFTSMDRSRSASHRSTRFAATFYDIETLKVIDEEWQRTQCSPRET
 CVEVASELGKSTNTFFKPPCVNVFCRGGCCNEESLICMNTTSYISKQLFEISVPLTSVP
 ELVPVKVANHTGCKCLPTAPRHPYSIIRRSIQIPEEDRCSHSKKLCPIDMLWDSNKCKCV
 LQEENPLAGTEDHSHLQEPALCGPHMMFDEDRCECVCKTPCPKDLIQHPKNCSCFEC
 KESLETCCQKHKLFPDTCSCEDRCPFHTRPCASGKTACAKHCRFPKEKRAAQGPHS
 RKNP

SEQ ID No:108

MMNNSGYSDAGLGLGDETDEMPSTEKDLAEDAPWKKIQQQNTFTRWCNEHLKCVGKRL
 TDLQRDLSDGLRLIALLEVLSQKRMYRKFHPRPNFRQMKLENVSVALEFLEREHIKLVSI
 DSKAIVDGNLKLILGLIWTLLHYSISMPWEDEDDEDARKQTPKQRLLGWIQNKPQLPI
 TNFNRDWQDGKALGALVDNCAPGLCPDWEAWDPNQPVENAREAMQQADDWLGPVQ
 VIAPEEIVDPNVDEHSVMTYLSQFPKAALKPGAPVRSKQLNPKKAIAYGPGIEPQGNTVL
 QPAHFTVQTVDAGVGEVLVYIEDPEGHTEEAKVVPNNKDRTYAVSYVPKVAGLHKVT
 VLFAGQNIERSPFEVNNGMALGDANKVSARGPGLEPVGNVANKPTYFDIYTAGAGTGD
 VAVVIVDPQGRRDTVEVALEDKG DSTFRCTYRPAMEGPHTVHAFAGAPI TRSPFPVH
 VSEACNPNACRASGRGLQPKGVRVKEVADFKVFTKGAGSGELKVTKGPKGTEEPVK
 VREAGDGVFECEYYPVVPKGYYVVTITWGGAIPRSPFEVQSPEAGVQKVRAWGPGL

ETGQVGKSADFVVEAIGTEVGLGFSIEGPSQAKIECDDKGDGSCDVRYWPTEPGEYA
VHVICDDEDIRDSPFIAHILPAPPDCFPDKVKAFCGPGLEPTGCIVDKPAEFTIDARAAGKG
DLKLYAQDADGCPIDIKVIPNGDGTFRCSYVPTKPIKHTIIISWGGVNPKSPFRNVGEG
SHPERVKVYGPVKEKTGLKANEPTYFTVDCSEAGQGDVSIGIKCAPGVVGPAEADIDFD
IICKNDNDTFTVKYTTPPGAGRVTIMVLFANQEIPASFHVKVDPSHDASKVKAEGPGLNRT
GVEVGKPTHFTVLTGAGKAKLDVQFAGTAKGEVVRDFEIIDNHDSYTVKYTAVQQG
NMAVTVTYGGDPVPKSPFVVNVAPPLDLISKVQGLNSKVAVGQEQAFAVNTRGAGG
QGQLDVRMTSPSRRPIPCKLEPGGGAEAQAVRYMPPEEGPYKVDITYDGHPVPGSPF
AVEGVLPDPDKVCAYGPGLKGGLVGTPAPFSIDTKGAGTGGLGLTVEGPCEAKIECQ
DNGDGSCAVSYLPTEPGEYTINILFAEAHIPSPFKATIRPVFDPSKVRASGPGLERGKV
GEAATFTVDCSEAGEAELTIEILSDAGVKAEVLIHNNADGTYHITYSPAFTGTYTITIKYGG
HPVPKFPTRVHVQPAVDTSGVKVSGPGVEPHGVREVTTFTVDARSLTATGGNHVTA
RVLNPSGAKTDYVTNDNGDGTYRVQYTAYEEGVHLVEVLYDEVAVPKSPFRVGVT
DPTRVRAFGPGLEGGLVNKANRFTVETRGAGTGGLGLAIEGPSEAKMSCKDNKDGS
TVEYIPFTPVDVNITFGGRPIPSPFRVPVKDVVDPGKVKCSGPGLGAGVRARVPQT
FTVDCSQAGRPLQAVLGPTGVAEPVEVRDNGDGTHTVHYTPATDGPYTVAVKYAD
QEVRSPFKIKVLPDASKVRASGPGLNASGIPASLPVEFTIDARDAGEGLLTVQILED
PEGKPKKANIRDNGDGTYSYLPDMSGRYTITIKYGGDEIPYSPFRIHALPTGDASKCL
TVSIGGHGLGACLGPRIQIGQETVITVDAKAAGEGKVTCTVSTPDGAELDVDV
ENHDGTFDIYYTAPEPGKYVITIRFGGEHIPNSPFHVLACDPLPHEEEPSEVPQLRQPYAPPRP
GARPTHWATEEPVVPVEPMESMLRPFLNLVIPFAVQKGELTGEVRMPSGKTARPNTDN
KDGTTVRYAPTEKGLHQMGIKYDGNHIPGPLQFYVDAINS
RHVSAYGPGLSHGMVNKPATFTIVTKDAGEEGGLSLAVEGPSKAEITCKDNKDG
CTVSYLPTAPGDYSIIVRFDDKHIPGSPFTAKITGDDSMRTSQLNVGTSTD
VSLKITESDLSQLTASIRAPSGNEEPCLLKRLPNR
HIGISFTPKEVGEHVVSVRKSGKHVTNSPFKILVGPSEIGDASKV
RVWGKGLSEGHTFQVAEFIVDTRNAGYGGGLSIEGPSKVDIN
CEDMEDGTCKVTCPTEPGTYIINIKFADKHVP
GSPFTVKVTGEGRMKESITRRRQAPSIATIGSTCDLN
LKIPGNWFQMVS
AQERLTRTFRSSHTYTRTERTEISKTRGGETKREVR
VEESTQVGGDPFP
AVFGDFLGRERLGSFGSITRQQE
GEASSQDMTAQVT
SPSGKVEAAE
IVEGEDSAYS
VRFVPQEMGP
HTVAVKYRGQH
VPGSPFQFTV
GPLGEGGA
HKV
RAGGT
GLERGV
VAGV
PAEFSI
WTREAGAGGL
IAVEGPS
KAEIA
FEDRK
DGSC
GVSY
VQEP
GDYE
VSIKF
NDE
HIP
DSPF
VVP
VASL
SDDA
RRLT
VTS
LQET
GLK
VNQP
ASFA
VQLNG
ARG
VIDAR
VHTPS
GAVE
EECY
VSEL
DSD
KHT
IRF
IPHENG
VHS
IDV
KFNGA
HIP
SPFK
IRV
GEQS
QAGDP
GLV
SAY
GPGL
EGGTT
GS
V
SSEFI
VNTLN
AGSG
ALS
VTID
GPSK
VQLDC
REC
PEGH
VVT
TPMA
PGNY
LIA
KYGG
PQHIVGS

PFKAKVTGPRLSGGHSLHETSTVLVETVKSSSSRGSSYSSIPKFSSDASKVVTRGPGL
 SQAFVGQKNSFTVDCSKAGTNMMMVGVHGPKPCEEVYVKHMGNRVYNVTYTVKEK
 GDYILIVKGDESPGSPFKVKVP

SEQ ID No:109

MDGASAEQDGLQEDRSHSGPSSLPEAPLKPPGPLVPPDQQDKVQCAEVNRASTEGES
 PDGPGQGGLCQNGPTPPFDPPSSLDPPTSPVGPDASPGVAGFHDNLRKSQGTSQEG
 SVRKEALQSLRLSLPMQETQLCSTDSPLEKEEQVRLQARKWLEEQLKQYRVKRQQE
 RSSQPATKTRLFSTLDPEMLNPNENLPRASTLAMTKEYSFLRTSVPRGPKVGSLGLPAH
 PREKKTSKSSKIRSLADYRTEDSNAGNSGGNVAPDSTK GSLKQNRSSAASVVSEISLS
 PDTDDRLENTSLAGDSVSEVDGNDSDSSYSSASTRGTYGILSKTVGTQDTPYMVNGQ
 EIPADTLGQFPSIKDVLQAAAEEHQDQQEVNGEVRSSRDSICSSVSLESSAAETQEEM
 LQVLKEKMRLEGQLEALSLEASQALKEKAELQAQLAALSTKLQAQVECSHSSQQRQDS
 LSSEVDTLKQSCWDLERAMTDLQNMLEAKNASLASSNNDLQVAEEQYQRLMAKVEDM
 QRSMILSKDNTVHDLRQQMTALSQLQQVQLERTTTSKLKASQAEISSLQSVRQWYQ
 QQLALAQEAVRLQGEMAHIQVGQMTQAGILEHLKLENVSLSQQLTETQHRSMKEKGR
 IAAQLQGIEADMIDQEAAFMQIQEAKTMVEEDLQRRLEEFEGERERLQRMADSAASLE
 QQLEQVKLTLLQRDQQLEALQQEHLDLMKQLTQEALQSREQSLDALQTHYDELQAR
 LGELQGEAASREDTICLLQNEKIILEAACQAKSGKEELDRGARRLEEGTEETSETLEKL
 REELAIKSGQVHELQQETAALKQMVKIKEQFLQQKVMVEAYRRDATSKDQLISELKAT
 RKRLDSELKELRQELMQVHGEKRTAEAEELSRLHREVAQVRQHMADLEGHLQSAQKER
 DEMETHLQLQFDKEQMVAVTEANEALKQIEELQQEARAKAITEQKQKMRRLGSDLTS
 AQKEMKTKHKAYENAVGILSRRLQEALAAKEAADAEGLQLRAQGGSSDSSLALHERIQA
 LEAEIQAQVSHSKTLLEKELQEVIALTSQELEESREKVLELEDELQESRGFRKKIKRLEES
 NKKLALELEHEKGKLTGLGQSNAALREHNSILETALAKREADLVQLNLQVQAVLQRKEE
 EDRQMKHLVQALQASLEKEKEKVNSLKEQVAAAKVEAGHNRHFKAASLELSEVKKEL
 QAKEHLVQKLQAEADDLQIREGKHSQEIAQFQAEAEARAQLQLLQKQLDEQLSKQPV
 GNQEMENLKWEVDQKEREIQSLKQQQLTEQQGRKELEGLQQLLQNVKSELEMAQED
 LSMTQDKDFMLQAKVSELKNMKTLLQQNQQQLKLDLRRGQDEKGAESAGQLFQPCHA
 HQDPGLPSSRLAAGGAAETTARREQGAPQEPEQLPPAAQAGDGQPAAPDGGARPDG
 ARVSVLVDAAGASHCQPCAPGGSRPRTTETQSEQGFQRRAGRVTAVDSPPCAA
 PEGSYQCYLFDCCVVDVFLRHEI

SEQ ID No:110

MAPIGLKAVVGEKIMHDVIKKVKKGEWKVLVDQLSMRMLSSCCKMTDIMTEGITIVED
 INKRREPLPSLEAVYLITPSEKSVHSLISDFKDPPATAKYRAAHVFTDSCPDALFNELVKS
 RAAKVIKTLEINIAFLPYESQVYSLDSADSFQSFSYSPHKAQMKNPLIERLAEQIATLCATL
 KEYPAVRYRGEYKDNLALLAQLIQDKLDAYKADDPTMGEGPDKARSQQLILDRGFDPSSP
 VLHELTFFQAMSYDLPPIENDVYKYETSGIGEARVKEVLLDEDDDLWIALRHKHIAEVSQE
 VTRSLKDFSSSKRMNTGEKTTMRDLSQMLKKMPQYQKELSKYSTHLHLAEDCMKHYQ
 GTVDKLCRVEQDLAMGTDAEGERIKDPMRAIVPILLDANVSTYDKIRIILLYIFLKNGITEE
 NLNKLIQHAQIPPEDSEIITNMAHLGVPIVTDSLRRRSKPERKERISEQTYQLSRWTPIIK
 DIMEDTIEDKLDTKHYPYISTRSSASFSTTAVSARYGHWHKNKAPGEYRSGPRLIIFILGG
 VSLNEMRCAYEVHQANGKWEVLIGSTHILTPTKFLMDLRHPDFRESSRVSFEDQAPTM
 E

SEQ ID No:111

MATGGYRTSSGLGGSTTDFLEEWKAKREKMRAKQNPPGPAPPGGGSSDAAGKPPAG
 ALGTPAAAAANELNNNLPGGAPAAPAVPGPGGVNCAVGSAMLTRAPPARGPRRSEDE
 PPAASASAAPPPQRDEEEDGVPEKGKSSGPSARKKGQIEKRKLREKRRSTGVVNIP
 AAECLEDEYEDDEAGQKERKREDAITQQNTIQNEAVNLLDPGSSYLLQEPPRTVSGRYK
 STTSVSEEDVSSRYSRTDRSGFPRYNRDANVSGTLVSSSTLEKKIEDLEKEVVTERQEN
 LRLVRLMQDKEEMIGKLKEEIDLNNRDLDDIEDENEQLQKENKTLKVVGQLTR

SEQ ID No:112

MKDRTQELRTAKDSDDDDDVAVTVDRDRFMDEFFEQQVEEIRGFIDKIAENVEEVKRKHS
 AILASPBPDEKTKEELEELMSDIKKTANKVRSKLKSIEQSIEQEEGLNRSSADLRIRKTQH
 STLSRKFVEVMSEYNATQSDYRERCKGRIQRQLEITGRTTSEELEDMLESGNPAIFAS
 GIIMDSSISKQALSEIETRHSEIIKLENSIRELHDMFMDMAMLVESQGEMIDRIEYNVEHAV
 DYVERAVSDTKKAVKYQSKARRKKIMIIICCVILGIVIASTVGGIFA

SEQ ID No:113

MKDRTQELRSAKDSDEEEVHVDRDHFMDEFFEQQVEEIRGCIEKLSEDVEQVKKQHS
 AILAAPNPDEKTQELEDLTADIKKTANKVRSKLKAIEQSIEQEEGLNRSSADLRIRKTQH
 STLSRKFVEVMTEYNATQSKYRDRCKDRIQRQLEITGRTTSEELEDMLESGKLAIFTDD
 IKMDSQMTKQALNEIETRHNEIIKLETSIRELHDMFVDMAMLVESQGEMIDRIEYNVEHS
 VDYVERAVSDTKKAVKYQSKARRKKIMIIICCVVLGVVLASSIGGTGL

SEQ ID No:114

MKDRLEQLKAKQLTQDDDTDAVEIAIDNTAFMDEFFSEIEETRLNIDKISEHVEEAKKLYS
 IILSAPIPEPKTKDDLEQLTTEIKKRANNVRNKLKSMEKHIEEDEVRSSADLRIRKSQHSVL
 SRKFVEVMTKYNEAQVDFRERSKGRIQRQLEITGKTTDEELEEMLESGNPAIFTSGIID
 SQISKQALSEIEGRHKDIVRLESSIKELHDMFMDIAMLVENQGEMLDNIELNVMHTVDHV
 EKARDESKKAVKYQSQARKKLIIIVLVVVLLGILALIIGLSVGLN

SEQ ID No:115

MNHLEGS A E V E T D E A A G G E V N E S V E A D L E H P E V E E E Q Q Q P P Q Q H Y V G R H Q R G R A
 LEDLRAQLGQEEEERGECLARSASTESGFHNHTDAEGDVIAAARDGYDAERAQDPED
 ESAYAVQYRPEAEYEQEAEAHAEATHRRALPNHLHFHSLEHEEAMNAAYSGYVYTH
 RLFHRGEDEPYSEPYADYGGLQEHVYEEIGDAPELDARDGLRLYEQERDEAAAYRQE A
 LGARLHHYDERSDGESDSPEKEAEFAPYPRMDSYEQEEDIDQIVAEVKQSMSSQSLDK
 AAEDMPEAEQDLERPPPTAGGRPDSPGLQAPAGQQRAVGPAGGGEAGQRYSKERKD
 AISLAIKDIKEAIEEVKTRTIRSPYTPDEPKEPIWVMRQDISPTRDCDDQRPMGDSPSP
 GSSSPLGAESSSTSLHPSDPVEVPINKESRKSLASFPTYVEVPGPCDPEDLIDGIIFAANY
 LGSTQLLSDKTPSKNVRMMQAQEAVSRIKMAQKLAKSRKKAPEGESQPMTEVDLFILT
 QRIKVLNADTQETMMDHPLRTISIYADIGNIVVLMAR R R I P R S N S Q E N V E A S H P S Q D G K R
 QYKMICHVFESEDAQLIAQSIGQAFSVAYQEFLRANGINPEDLSQKEYSDLLNTQDMYN
 DDLIHFSKSENCKDVFIEKQKGEILGVVIVESGWGSILPTVIIANMMHGGPAEKSGKLNIG
 DQIMSINGTSVLGPLSTCQSIIGLENQSRVKLNIVRCPPVTVLIRR PDLRYQLGFSVQ
 NGIICSLMRGGIAERGGVRVGHRIIEINGQSVVATPHEKIVHILSNAVGEIHMKTPAAMY
 RLLTAQEQPVYI

SEQ ID No:116

MALADSTRGLPNGGGGGGGSSSSSAEPLLFDIVELNVGGQVYVTRRCTVVSPD
 SLLWRMFTQQQPQELARDSKGRFFLDRDGFLFRYILDYLRLQLVLPDYFPERSRLQR
 EA EYFELPELVRRLGAPQQPGPGPPPSRRGVHKEGSLGDELLPLGYSEPEQQEGASA
 GAPSPTELASRSPSGGAAGPLLTPSQSLGSRRSGYITIGYRGSYTIGRDAQADAKFR
 RVARITVCGKTS LAKEVFGDTLNESRDPDRP PERYTS RYYLKFNFLEQAFDKLSESGFH
 MVACSSGTCAFASSTDQSEDKIWTSYTEYVFCRE

SEQ ID No:117

MVMLLLSALAGLFGAAEGQAFHLGKCPNPPQENFDVNKYLGRWYEIEKIPTTFENG
RCIQANYSLMENGKIKVLNQELRADGTVNQIEGEATPVNLTEPAKLEVKFWSFMPSPAPY
WILATDYENYALVYSCTCIQLFHVDFAWILARNPNLPPETVDSLKNILTSNNIDVKKMTVT
DQVNCPKLS

SEQ ID No:118

MLGGSGSHGRRSLAALSQIAQRNDDDEEEAARERRRARQERLRQKQEEESLGQVT
DQEVNAQNSVPDEEAKTTTNTQVEGDDEAFLERLARREERRQKRLQEALERQKEF
DPTITDASLSPSRRMQNDTAENETTEKEEKSESQRQERYEIEETETVTKSYQKNDWRDA
EENKKEDKEKEEEEEPKRGSIGENQGEEKGTKVQAKREKLQEDKPTFKKEEIKDEKI
KKDKEPKEEVKSFMDRKKGFTEVKSQNQEFMTHKLKHTENTFSRPGGRASVDTKEAE
GAPQVEAGKRLEELRRRRGETESEEFELKQKQQAALELEELKKKREERRKVLEEEE
QRRKQEEADRKLREEEKRRRKEEIERRRAEAAEKRQKMPEDGLSDDKKPFKCFTPKG
SSLKIEERAFLNKSVQKSSGVKSTHQAAIVSKIDSRLEQYTSIAEGTKSAKPTKPAASDL
PVPAEGVRNIKSMWEKGNVFSSPTAACGTPNKETAGLKVGVSSRINEWLTKTPDGNKSP
APKPSDLRPGDVSSKRNLWEKQSVDKVTSPKV

SEQ ID No:119

MLLSVPLLLGLLAVALAEPAVYFKEQFLDGDGWTSRWIESKHKSDFGKFVLSSGKFY
DEEKDKGLQTSDARFYALSASFEPFSNKGQTLVVQFTVKHEQNIDCGGGYVKLFNS
LDQTDMHGDSEYNIMFGPDICGPGBTKKVHVIFNYKGKNVLINKDIRCKDDEFTHLYTLIV
RPDNTYEVKIDNSQVESGSLEDDWDFLPPKKIKDPDASKPEDWDERAKIDDPTDSKPE
DWDKPEHIPDPDAKKPEDWDEEMDGEWEPPVIQNPEYKGEWKPRQIDNPDYKGTWIH
PEIDNPEYSPDPSIYAYDNFGVLGLDWQVKSGTIFDNFLITNDEAYAEEFGNETWGVT
AAEKQMVKQDEEQRLKEEEEKKRKEEEEADKEDDEDKDEDEEDEEDKEEDEED
VPGQAKDEL

SEQ ID No:120

MLGLRPPLLALVGLLSLGCVLSQECTKFKVSSCRECIESGPGCTWCQKLNFTGPGDPD
SIRCDTRPQLLMRGCAADDIMDPTSLAETQEDHNGGQKQLSPQKVTLYLRPGQAAAFN
VTFRRAKGYPIDLYLMDLSYSMLDDLNVKKLGGDLLRALNEITESGRIGFGSFVDKTV
LPFVNTHPDKLRNPCPNKEKECQPPFAFRHVLKLTNNNSNQFQTEVGKQLISGNLDAPE
GGLDAMMQVAACPEEIGWRNVTRLLVFATDDGFHFAGDGKLGAILTPNDGRCHLEDNL
YKRSNEFDYPSVGQLAHKLAENNIQPIAVTSRMVKTYEKLTEIIPKSAVGELSEDSSNV

VHLIKNAYNKLSSRVFLDHNALPDTLKVTYDSFCNSGVTHRQNQPRGDCDGVQINVPIF
 QVKVTATECIQEASFVIRALGFTDIVTVQVLPQCECRCDQSRSRSLCHKGFLFCGIC
 RCDTGYIGKNCECQTQGRSSQELEGSCRKDNNSIICSGLGDCVCGQCLCHTSVDVPGKL
 IYGQYCECDTINCERYNGQVCGGPGRGLCFGKCRCHPGFEWSACQCERTTEGCLNP
 RRVECSGRGRCRCNVCECHSGYQLPLCQECPGCPSPCGKYISCAECLKFEKGPFKGK
 CSAACPGLQLSNNPVKGRTCKERDSEGCWVAYTLEQQDGMDRYLIYVDESERCVAGP
 NIAAIVGGTVAGIVLIGILLVIWKALIHLSDLREYRRFEKEKLKSQWNNDNPLFKSATTTV
 MNPKFAES

SEQ ID No:121

MWRLRRAAVACEVCQSLVKHSSGIKGSPLQKLHLVSRSIYHSHHPTLKLQRPQLRTSF
 QQFSSLTNLPLRKLKFSPIKYGYQPRRNFWPARLATRLLKLRYLILGSAVGGGYAKKTF
 DQWKDMIPDLSEYKWIVPDIWWEIDEYIDFGSPEETAFRATDRGSESCHKFRKGLLGELI
 LLQQQIQEHEEEARRAAGQYSTSQAQQKRKVSDKEIDQLQEELLHTQLKYQRILERLE
 KENKELRKVLQKDDKGIIHRKLKKSIDMYSEVLDVLSDYDASYNTQDHLPRVVVGD
 QSAGKTSVLEMIAQARIFPRGSGEMMTRSPVKVTLSEGPHVALFKDSSREFDLTKEED
 LAALRHEIELRMRKNVKEGCTVSPETISLNVKGPGLQRMVLVDLPGVINTVTSGMAPDT
 KETIFSISKAYMQNPNAIILCIQDGGSVDAERSIVTDLVSQMDPHGRRTIFVLTKVDAEKN
 VASPSRIQQIIEGKLFPMKALGYFAVVTGKGNSSESIEAIREYEEEFFQNSKLLKTSMLKA
 HQVTTRNLSLAWSDCFWMVRESVEQQADSFKATRFNLETEWKNNYPRLRELDRNEL
 FEKAKNEILDEVISLSQVTPKHWEELQQLWERVSTHVIENIYLPAATQMNSGTNTTV
 DIKLKQWTDKQLPNKAVEVAWETLQEEFSRFMTEPKGKEHDDIFDKLKEAVKEESIKRH
 KWNDFAEDSLRVIQHNALEDRSISDKQQWDAAIYFMEEALQARLKDTENAIENMVGPD
 WKWRWLYWKNRTQEQQCVHNETKNELEKMLKCNEEHPAYLASDEITTVRKNLESRGVE
 VDPSLIKDTWHQVYRRHFLKTALNCNLRRGFYYQRHFVDSELECNDFVLFWRIQR
 MLAITANTLRQQLTNTEVRRLEKNVKEVLEDFAEDGEKKIKLLTGKRVQLAEDLKKVREI
 QEKLDAFIEALHQEK

SEQ ID No:122

MLSQVYRCGFQPFNQHLLPWVKCTVFRSHCIQPSVIRHVRWSNIPFITVPLSRTHGK
 SFAHRSELKHAKRIVVKLGSAVTRGDECGLALGRLASIVEQVSVLQNQGREMMLVTS
 GAVAFGKQRLRHEILLSQSVRQALHSGQNQLKEMAIPVLEARACAAAGQSGLMALYEAM
 MFTQYSICAAQILVTNLDHDEQKRRNLNGTLHELLRMNIVPIVNTNDAVVPPAEPNSDL
 QGVNVISVKDNDLSAARLAVEMKTDLLIVLSDVEGLFDSPPGSDDAKLIDIFYPGDQQSV

TFGTKSRVGMGGMEAKVKAALWALQGGTSVVIANGTHPKVSGHVITDIVEGKKVGTFF
 SEVKPAGPTVEQQGEMARSGGRMLATLEPEQRAEIIHHLADLLTDQRDEILLANKKDLE
 EAEGRLAAPLLKRLSLSTKLNSLAIGLRQIAASSQDSVGRVLRRTRIAKNLEEQVTVP
 GVLLVIFESRPDCLPQVAALAIASGNGLLKGGKEAAHSNRILHLLTQEALSIHGKVKEAVQ
 LVNTREEVEDLCRLDKMIDLIIIPRGSSQLVRDIQKAAKGIPVMGHSEGICHMYVDSEASV
 DVKTRLVRDSKCEYPAACNALETLLIHRDLLRTPLFDQIIDMLRVEQVKIHAGPKFASYLT
 FSPSEVKSLRTEYGDLELCIEVVVDNVQDAIDHIHKYGSSHTDVIVTEDENTAEFFLQHVD
 SACVFWNASTRFSDGYRFGLGAEVGISTSRIHARGPVGLEGLTTKWLLRGKDHHVSD
 FSEH GSL KYLHENLPIPQRNTN

SEQ ID No:123

MTELPAPLSYFQNAQMSEDNHL SNTNDNRERQEHNDRRS LGHPEPLSNGRPQGNSR
 QVVEQDEEEDEELTLKYGAKHVIMLFVPTLCMVVVVATIKSVSFYTRKDQQLIYTPFTE
 DTETVGQRALHSILNAAIMISVIVVMTILLVVLYKYRCYKVIHAWLISSLLLLFFSFYLGE
 VFKTYNVAVDYITVALLIWNLGVVGMISIHWGPLRLQQAYLIMISALMALVFIKYLPEWT
 AWLILAVISVYDLVAVLCPKGPLRMLVETAQERNETLFPALIYSSTMVWL VNMAEGDPEA
 QRRVSKNSKYNAESTERESQDTVAENDDGGFSEEWEAQRDSHLGPHRSTPESRAAV
 QELSSSILAGEDPEERGVKLGDFIFYSVLVGKASATASGDWNTTIACFVAILIGLCLTL
 LLLAIFKKALPALPISITFGLVFYFATDYLVQPFMDQLAFHQFYI

SEQ ID No:124

MSTGGDFGNPLRKFKLVFLGEQSVGKTSLITRFMYDSFDNTYQATIGIDFLSKTMYLED
 RTVRLQLWDTAGQERFRSLIPSYIRDSTVAVVYDITNVNSFQQTTKWIDDVRTERGSD
 VIIMLVGNKTDLADKRQVSIEGERKAKELNVMFIETS A KAGYNVKQLFRRVAAALPGME
 STQDRSREDMIDI KLEKPQEQPVSEGGCSC

SEQ ID No:125

MADNLSDTLKKLKITA VDKTEDSLEGCLDC LLQALAQNNTETSEKIQASGILQLFATLLTP
 QSSCKAKVANIIAEVAKNEFM RIPCV DAGLISPLVQLLNSKDQEVLQTGRALGNICYDS
 HEGRSAVDQAGGAQIVIDHLRSLCSITDPANEKLLTVFCGMLMNYSNENDSLQAQLINM
 GVIPTLVKLLGIHCQNA ALTEMCLVAFGNLAELESSKEQFASTNIAEELV KLFKKQIEHDK
 REMIFEVLA PL AENDAIK LQLVEAGLVECLL EIVQQKV DSDKEDDITELKTGSDLMVLLL
 GDESMQKLFE GGKGSVQRVLSWIPSNNHQLQLAGALAIANFARNDANC IHMVDNGIV
 EKLMDLLDRHVEDGNVTVQHAALSALRNLAIPVINKAKMLSAGVTEAVLKFLKSEMPPV

QFKLLGTLRMLIDAQEAAEQLGKNVKLVERLVEWCEAKDHAGVMGESNRLLSALIRHSK
 SKDVIKTIVQSGGIKHLVTMATSEHVIMQNEALVALALIAALELGTAEKDLESAKLVQILHR
 LLADERSAPEIKYNNSMVPLICALMGSECLHKEVQDLAFLDVSKLRSHENKSVAQQASLT
 EQRLTVES

SEQ ID No:126

MPGPSPGLRRALLGLWAALGLGLFGLSAVSQEPFWADLQPRVAFVERGGSLWLNCST
 NCPRPERGGLETSLRRNGTQRGLRWLARQLVDIREPETQPVCFFRCARRTLQARGLIR
 TFQRPDRVELMPLPPWQPVGENDFTLSCRVPAGPRASLTLLRGAQELIRRSFAGEP
 PRARGAVLTATVLARREDHGANCRAELDLRPHGLGFENSSAPRELRTFSLSPDAP
 RLAAPRLLEVGSERPVSCLDGLFPASEARVYALGDQNLSPDVTLEGDAFVATATA
 SAEQEGARQLVCNVTLGGENRETRENTIYSFPAPLLTSEPSVSEGQMVTCAAGA
 QALVTLEGVPAAVPGQPAQLQLNATENDRRSFFCDATLDVDGETLIKNRSAELRVLYA
 PRLDDSDCPRSWTPEGPEQTLRCEARGNPEPSVHCARSDGGAVLALGLGPVTRAL
 SGTYRCKAANDQGEAVKDVTLTVEYAPALDSVGCPERITWLEGTEASLSCVAHGVPPP
 DVICVRSGELGAVIEGLRVAREHAGTYRCEATNPRGSAAKNVAVTVEYGPRFEEPSCP
 SNWTWVEGSGRLFSCEDGKPQPSVKVGSGGTTEGVLLPLAPPDPSPRAPRIPRVL
 -APGIYVCNATNRHGSVAKTVVSAESPPEMDESTCPHQTWLEGAEASALACAARGR
 PSPGVRCSCREGIPWPEQQRVSREDAGTYHCVATNAHGTDRTVTGVEYRPVVAELA
 ASPPGGVRPGGNFTLCRAEAWPPAQISWRAPPRALNIGLSSNNSTLSVAGAMGSHG
 GEYECARTNAHGRHARRITVRVAGPWLWAVGGAAGGAALLAAGAGLAFYVQSTACK
 KGEYNVQEAESSGEAVCLNGAGGGAGGAAGAEGGPEAAGGAAESPAEGEVFAIQLTS
 A

SEQ ID No:127

MAAGPSGCLVPAFGLRLLLATVLQAVSAFGAEFSSEACRELGFSSNLLCSSCDLLGQFN
 LLQLDPDCRGCCQEEAQFETKKLYAGAAILEVCGCKLGRFPQVQAFVRSDFPKLFRGLQI
 KYVRGSDPVLKLLDDNGNIAEELSILKWNTDSVEEFLSEKLERİ

SEQ ID No:128

MDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSI
 HHGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN

SEQ ID No:129

MAQALPWLLWMGAGVPAHGTQHGIRLPLRSGLGGAPLGLRLPRETDEEPEEPGR
 GSFVEMVDNLRGKSGQQGYYVEMTVGSPPQTLNILVDTGSSNFAVGAAPHFLHRYYQ
 RQLSSTYRDLRGVYVPTQGKWEGETLVSIPHGPNTVRANIAITESDKFFINGS
 NWEGILGLAYAEIARPDDSLEPFFDSLVKQTHVPNLFLQLCGAGFPLNQSEVLASVGG
 SMIIGGIDHSLYT GSLWYTPIRREWYYEVIVRVEINGQDLKMDCKE NYDKSIVDSGTTN
 LRLPKKVFEAAVKSIAASSTEKFDPFWLGEQLVCWQAGTPWNIFPVISLYLMGEVT
 NQSFRITILPQQYLRPVEDVATSQDDCYKFAISQSSTGTVMGAVIMEGFYVVFDRARKRI
 GFAVSACHVHDEFRTAAVEGPFTLDMEDCGYNIPQTDESTLMTIAYVMAAICALFMLP
 LCLMVCQWRCLRCLRQQHDDFADDISLLK

SEQ ID No:130

MPKGRQKVPHLDAPLGLPTCLWLELAGLFLLVPWVMGLAGTGGPDGQGTGGASWAV
 HLESLEGDGEETLEQQADALAQAAGLVNAGRIGELQGHYLVQPAGHRPALEVEPIR
 QQVEAVLAGHEAVRWHSEQRLLRRAKRSVHFNDPKYPQQWHLNNRRSPGRDINV
 VWERNVTRGVTVVVVDDGVEHTIQDIAPNYSPEGSYDLNSNDPDPMPHPDVENG
 HGTRCAGEIAAVPNNSFCAVGVAYGSRIAGIRVLDGPLTDMSMEAVAFNKHYQINDIYSCS
 WGPDDDGKTVDPHQLGKAALQHGVIAQRQGFGSIFVVASGNQQHNDNCNYDG
 NSIYTVTIGAVDEEGRMPFYAEECASMLAVTFSGGDKMLRSIVTTDWDLQKGTGCTEG
 HTGTSAAAPLAAGMIALMLQVRPCLTWRDVQHIIIFTATRYEDRRAEWVTNEAGFSHS
 HQHGFGLNAWRLVNAAKIWTSPYLASYVSPVLKENKAIPQSPRSLEVWNVS
 RMDLEMISGLKTLEHVAVTVSITHPRRGSL
 ELELKLCPSGMMMSLIGAPRSMDSDP
 NGFNDWTFS
 TVRCWGERARGTYRLVIRDVGDES
 FQVGILRWQLTLYGSVWSAVDIRDRQR
 LLESAM
 SGKYLHDDFALPCPPGLKIPEEDGY
 TITPNTLKTLVLCFTVF
 WT
 VYYMLEVYLSQRNV
 ASNQVCRSGPCHWPHRSRKA
 KEEGTELESVPLCSSKDP
 DEVETESRGPP
 TSDLLAP
 DLLEQGDWSLSQNKSALDCPHQHLDVPHGKEEQIC

SEQ ID No:131

GGGSCRGRGLQRASGLRARRGLERQTAQWA
 EKEAQQPPWPV
 MEMEKEFEQIDKSG
 SWAAIYQDIRHEASDFPCRVAKLPKNKNRNR
 YRDVSPFDHSRIKLHQEDNDYINASLIK
 MEEAQRSYILTQGPLNT
 CGHF
 WEMVWEQKSRGV
 VMLNRV
 MEKSLKCAQYWPQKE
 EKEMIFEDTNLKLTL
 ISED
 IKSY
 YTVRQLE
 LENLT
 QTREILHF
 HYTT
 PDFGVP
 ESPAS
 FLNFLFKVRES
 GSLSPE
 HGP
 VV
 HCSAGI
 GRSGT
 FCLADT
 CLLL
 MDKR
 KDP
 SSVDIKK
 V
 LLEMRKFRMGLI
 QTAD
 QLRF
 SYLAV
 IE
 GAKF
 IMGDSS
 VQDQW
 KELSHED
 LEPP
 PEHIPP
 PPRPPKRILE
 PHNG
 KCREF
 FPNH
 QWV
 KEET
 QED
 KDC
 PIKEE
 KGSP
 LNAAP
 PYGIES
 MSQ

DTEVRSRVVGGLRGAQAAASPAKGEPESLPEKDEDHALSYWKPFLVNMCVATVLTAGA
YLCYRFLFNSNT

SEQ ID No:132

MEARVERAVQKRQVLFLCVFLGMSWAGAEPLRYVAEETERGFLTNLAKDLGLGVGE
LRARGTRIVSDQNMQILLSSLTGDLLNEKLDREELCGPREPCVLPFQLLEKPFQIFRA
ELWVRDINDHAPVFLDREISLKILESTTPGAFLLESAQDSDVGTNSLSNYTISPNAFYHI
NVHDSGEGNIYPELVLNQVLDREEIPEFSLTALDGGSPRGSGTALVRIIVLDVNDNAP
DFVRSLYKVQVPENSPVGSMVVSVSARDLDTGSNGEIAYAFSYATERILKTFQINPTSG
SLHLKAQLDYEAIQTYTLTIQAKDGGGLSGKCTVVVDVTDINDNRPELLSSLTPIAENS
PETVVAVFRIRDRDGSNNNGKTVCASIQQDPFILKPSVENFYTLVTEKPLDRERNTEYNITI
TVTDLGTPRLKTEHNITVLVSDVNDNAPAFQTSYTLFVRENNSPALPIGSVSATDRDSG
TNAQVIYSLPSQDPHLPLASLVSINADNGHLFALRSLDYEALQAFEFRVGATDRGSPAL
SSEALVRVLVLDANDNSPFVLYPLQNSSAPCTEPLPRAAEPGYLVTKVVAVDGDSGQN
AWLSYQLLKATEPGLFGVWAHNGEVRTARLLSERDAAKQRLVVLVKDNGEPPRSATAT
LHVLLVDGFSQPYLRLPEAAPDQANSLTVALASVSSLFLLSVLLFVAVRLCRRSRA
APVGRCSVPEGPFPRHLVDLSGTGTLSQSYQYEVCLGGSGTNEFKFLKPIIPNLLPQS
TGREVEENRPFQNNLGF

SEQ ID No:133

MDPLFQQTHKQVHEIQSCMGRLETADKQSVHIVENEIQASIDQIFSRLERLEILSSKEPP
NKRQNARLRVDQLKYDVQHLQTALRNQFHRRHAREQQERQRELLSRTFTNDSDTI
PMDESLQFNSSLQKVHNGMDDLILDGHNILDGLRTQRLTLKGTQKKILDIANMLGLSNTV
MRLIEKRAFQDKYFMIGGMLLTCVVMFLVVQYLT

SEQ ID No:134

MDNSGKEAEAMALLAEAERKVKNQSFFSGLFGGSSKIEEACEIYARAANMFMAKNW
SAAGNAFCQAAQLHLQLQSKHDAATCFVDAGNAFKKADPQEAINCLMRAIEIYTDMGRF
TIAAKHHISIAEIYETELVDIEKAIAHYEQSADYYKGEESNSSANKCLLKAGYAALEQYQ
KAIIDIYEQVGTNAMDPLLKYSAKDYFFKAALCHFCIDMLNAKLAVQKYEELFPAFSDSR
ECKLMKKLLEAHEEQNVDSYTESVKEYDSISRLDQWLTTMLLRIKKTIQGDEEDLR

SEQ ID No:135

MSVPSSLSQSAINANSHGGPALSPLPLHAAHNQLNAKLQATAVGPKDLRSAMGE GG
 GPEPGPANAKWLKEGQNQLRRAATAHRDQRNRNTLTLAEEASQEPEMAPLGPKGLIHL
 YSELELSAHNAANRGLRGPGLIISTQEQQPDEGEEEKAAAGEAEAAAAEDDDDEEEEEDLS
 SPPGLPEPLESVEAPPRPQALTDGPREHSKSASLLFGMRNSAASDEDSSWATLSQGSP
 SYGSPECEDTDSFWNPNAFETDSDPAGWMRVQDTSGTYYWHPTGTTQWEPPGRASP
 SQGSSPQEESQLTWTGFAHGEGFEDGEFWKDEPSDEAPMELGLKEPEEGTLTFFPAQS
 LSPEPLPQEEEKLPRTNPGIKCFAVRSLGWVEMTEELAPGRSSVAVNNCIRQLSYH
 KNNLHDPMSSGGWGEVKDLLLQLEDETLKLVEPQSQALLHAQPIISIRVGWGRDSGRE
 RDFAYVARDKLTQMLKCHVFRCEAPAKNIATSLHEICSKIMAERRNARCLVNGLSDLHS
 KLDVVFQVEFPAPKNELVQKFQVYLYGNPVAKPVGVDVINGALESVLSSSSREQWT
 PSHVSVAPATLTLHQQTTEAVLGECRVFLSFLAVGRDVHTFAFIMAAGPASFCCHMFW
 CEPNAASLSEAVQAACMLRYQKCLDARSQASTSCLPAPPAESVARVGVTVRRGVQS
 LWGSLKPRLGAHTP

SEQ ID No:136

MAAPQDVHVRICNQEIVKFDLEVKALIQDIRDCSGPLSALTELNTVKKEKFQQLRHRIQD
 LEQLAKEQDKESEKQLLQEVENHKKQMLSNNQASWRKANLTCKIAIDNLEKAELLQGGD
 LLRQRKTTKESLAQTSSTITESLMGISRMMAQQVQQSEEAMQSLVTSSRTILDANEELFK
 SMSGTIQLGRKLITKYNRRELTDKLLIFLALRLFLATVLYIVKKRLFPFL

SEQ ID No:137

MRRAGLGEVPPGNYGNYGYANSGYSACEEENERLTESLRSKVTAIKSLSIEIGHEVKT
 QNKLLAEMDSQFDSTTGFLGKTMGKLKILSRGSQTKLLCYMMLFSLFVFFIIYWIILKR

SEQ ID No:138

MFLVNSFLKGGGGGGGGGGGGGGGGGNLGVGGLISGAGGGGGGGGGGGGGGGGGGG
 GGTAMRILGGVISAISEAAAQYNPEPPPPRTHYSNIEANESEEVRQFRRLFAGDDM
 EVSATLMNILNKVTRHPDLKTDGFGIDTCRSMVAVMDSDTTGKLGFEFKYLWNNIK
 RWQAIYKQFDTDRSGTICSELPGAFEAAGFHLNEHLYNMIIIRRYSDESGNMDFDNFIS
 CLVRLDAMFRAFKSLKDGTGQIQVNIQEWLQLTMYS

SEQ ID No:139

MASFVTEVLAHSGRLEKEDLGTRISRLTRRVEEIKGEVCNMISKYSEFLPSMQSAQGLI
 TQVDKLSEDIDLLKSRIESEVRRDLHVSTGEFTDLKQQLERDSVVLSSLLKQLQEFSTAIEE

YNCALTEKKYVTGAQRLEEAQKCLKLLKSRKCFDLKILKSLSMELTIQKQNILYHLGEW
 QKLIVWKFPPSKDTSSLESYLQTELHLYTEQSHKEEKTPMPPPISSVLLAFSVLGEHLHSKL
 KSFGQMLLKYLRLPLASCPSLHAVIESQPNIVIIRFESIMTNLEYPSPSEVFTKIRLVLEVQ
 KQLLDLPLDLENEKTSTVPLAEMLGDMIWEDLSECLIKNCLVYSIPTNSSKLQQYEEII
 QSTEEFENALKEMRFLKGDTTDLLKYARNINSHFANKKCQDVIVAARNLMTSEIHNTVKII
 PDSKINVPELPTPDEDNKLEVQKVSNQYHEVMNLEPENTLDQHSFSLPTCRISESVKK
 LMELAYQTLLEATTSSDQCAVQLFYSVRNIFHLFHDVVPTYHKENLQKLPQLAAIHNNC
 MYIAHHLLTGHQFRLRLAPILCDGTATFVDLVPGFRRLGTECFLAQMRQAQKGELLRLS
 SAR NFS NM DEE NY SA ASK AVR QVL HQL KRL GIV W QD VLP V NI Y CK AM GT LL NTA I SEV
 IG KITA LE DI STE DG DRL Y SL C KTV M D E GP QV F APL S E E SKN K KY Q E E V P V Y VPK W MPF
 KELMMMLQASLQEIGDRWADGKGPLAAFSSSEVKALIRALFQNTERRAAALAKIK

SEQ ID No:140

MADPKYADLPGIARNEPDVYETSDLPEDDQAEGDAEELSTSVEHIVNPNAAYDKFKDK
 RVGTKGLDFSDRIGKTKRTGYESEGEYEMLGEGLVKETPQQKYQRLLHEVQELTTEVE
 KIKTTVKE SATEEKLTPVLLAKQLAALKQQLVASHLEKLLGPDAAINLTDPDGALAKRLLL
 QLEATKNSKGSGGKTTGTPPDSSLVTYELHSRPEQDKFSQAAKVAELEKRLTELETA
 VRCDQDAQNPLSAGLQGACLMETVELLQAKVSALDLAVLDQVEARLQSVLGVNEIAK
 HKASVEDADTQSKVHQLYETIQRWSPIASTLPELVQRLVTIKQLHEQAMQFGQLLTHLD
 TTQQMIANSLKDN TLLTQVQTTMRENLATVEGNFASIDERMKKLGK

SEQ ID No:141

MRTLLLVLWLATRGSA LYFHIGETEKCFIEEIPDET M VIGNYRTQLYDKQRE EYQPATP
 GFGMCVEVKDPEDKVILAREYGSEG RFTFTSHTPGEHQICLHSNSTKFSLFAGGMLRV
 HLDIQVGEHANDYAEIPAKDKLSELQLRVRQLVEQVEQI QKEQNYQRWREERFRQTSE
 STNQRVLWWSILQTLILVAIGVWQMRHLKSFFEAKKLV

SEQ ID No:142

MASSGAGDPLDSKRGEAPFAQRIDPTREKLTPEQLHS MRQAELAQWQKVLP RRTRNI
 VTGLGIGALVLAIYGTFYSISQERFLDELEDEAKAARALARASGS

SEQ ID No:143

KAPGSETKATRPGAWPTPGTSTPRPRKWLSARARVSRSIQLSTGRRTLLLTSAGAETV
 RTSLGTRRRRAPRFCPTSAWGSGPARMRAARRGLHCAGAERP RRRGRLWDSSGVP

QRQKRPGPWRTQTQEQQMSRDVCIHTWPCTYLEDPKRRWVTGQLSLTSLRFMTDST
 GEILVSFPLSSIVEIKKEASHFIFSSITILEKGHAKHWFSSLRPSRNVVFSIIEHFWRELLS
 QPGAVADASVPRTRGEELTGLMAGSQKRLED TARVLHHHQGQQLDSVMRG LDKMESD
 LEVADRLLTELESPA WWWPFSSKLWKTTPETKPREDVSMTSCEPFGKEGILIKIPAVISHR
 TESHVKPGRLTVLVSGLIEHDSSSLMHRFEREDVDDIKVHSPYEISIRQRFIGKPD MAY
 RLISAKMPEVPILEVQFSKKMELLEDALVRSARTSSPAEKSCSVWHAASGLMGCTLHR
 EPPAGDQE GTALHLQTSLPALSEADTQELTQILRRMKGLALEAESELERQDEALDGVA A
 AVDRATLTIDKHNR RMKRLT

SEQ ID No:144

SKSPGAQFPEAVSSERSSCTVVSQVCESPTMSASGVLSFTQQGWEQVLAKVKRAV VY
 LDAACAESLHWGCGSTRLLAEVGGPDCHLREFEPDAIGGGAKQP KAVFVLSCLLKG RT
 VEILRDIICRSHFQYCVVTTVSHAVHLTANHPA AAAAMEGQQPVFEQLEEKLC EWM
 GNMNYTAEVFHVPPLLAPVAPHFALTPAFASLFPLLPQDVHLLNSARPDKRKLGS LGDV
 DSTTLTPELLQIRCLVSGLSSLCEHLGVREECFAVGSL SQVIAADLANYAPAKNR KKTA
 AGRASVVFDRTLDLTGAVGHGDNLVEKIISALPQLPGHTNDVMVN MIALTALHTEEE
 NYNVVAPGCLSQSSDTTAKALWEALLNTKHKEAVMEVRRHLVEAASRENLPKMSMGR
 VTPGQLMSYIQLFKNNLKALMNHCGLLQLGLATAQTLKHP QTAKWDNFLA FERLLLQSI
 GESAMSVVLNQLLPMIKPVTQRTNEDYSPEELLILLIYIY SVTGE LTVDKDLCEAEEKVKK
 ALAQVFCEESGLSP LLQKITDWDSSINLT FHKS KIAVDELF SLRDIAGAR SLLKQFK SVY
 VPGNHTHQASYKPLLKVQVVEEIFHPERPDSVDIEHMSSGLTDLLKTGF S FMK VSR PHP
 SDYPLLILFVVGGTVSEVKMVKDLV ASLKPGTQVIVLSTRLLKPLNIPELLFATDRLHPD
 LGF

SEQ ID No:145

MAASRLELNVRLLSRCEAMAAEKRDPDEWRLEKYVGA LEDMLQALKVHASKPASEVI
 NEYSWKVDFLKGM LQAEKLTSSSEKALANQFLAPGRVPTT ARER VPATKTVHLQSRAR
 YTSEMRSELLG TD SAEPEMDVRKRTGVAGSQPVSEKQSAAELDVLQRHQNLQE KLA
 EEMLGLARS LKTNTLAAQSVIKKD NQ TLHS LK MADQNLEKLKTESERLEQHTQK SVN
 WLLWAMLII VCFIFISMILFIRIMP KLK

SEQ ID No:146

MVDQLEQILSVSELLEKHGLEKPISFVKNTQSSSEEARKLMVRLTRHTGRKQPPVSE SH
 WRTLLQDM LTMQQNVYTCLSDAC YEIFTESLLCSSRLEN ILAGQMMHCSACSENPP

AGIAHKGKPHYRVSYEKSIDLVLAASREYFNSSTNLTDSCMDLARCCLQLITDRPPAIQE
 ELDLIQAVGCLEEFVIELPLQVRLCPDRISLIKECISQSPTCYKQSTKLLGLAELLRVAGE
 NPEERRGQVLILLVEQALRFHDYKAASMHCQELMATGYPKSWDVCSQLGQSEGYQDL
 ATRQELMAFALTHCPPSSIELLLAASSSLQTEILYQRVNPFQIHEGGENISASPLTSKAVQ
 EDEVGVPGSNSADLLRWTTATTMKVLSNTTTKAVLQAVSDGQWWKSLTYLRPLQ
 GQKCGGAYQIGTTANEDLEKQGCHPFYESVISNPFAESEGTYDTYQHVPVESFAEVLL
 RTGKLAEAKNKGEVFPTTEVLLQLASEALPNDMTLALAYLLALPQVLDANRCFEKQSPS
 ALSLQLAAYYYSLQIYARLAPCFRDCKCHPLYRADPKELIKMVTRHVTRHEHEAWPEDLIS
 LTKQLHCYNERLLDFTQAQILQGLRKGVDVQRFTADDQYKRETIILGLAETLEESVYSIAIS
 LAQRYSVSRWEVFMTHLEFLFTDSGLSTLEIENRAQDLHLFETLKTDPEAFHQHMVKYI
 YPTIGGFIDHERLQYYFTLLENCGCADLGNCAIKPETHIRLLKKFKVVASGLNYKKLTDEN
 MSPLEALEPVLSSQNILSISKLVPKIPEKGQMLSPSSLYTILQKLFWTGDPHLIKQVPG
 SSPEWLHAYDVCMDKYFDRLHPGDLITVVDAVTFSPIAVTKLSVEARKEMTRKAIKTVKH
 FIEKPRKRNSEDEAQEAQDKVTVYADTLNHLKSLAHLETLSHSFILSKNSEQETLQKY
 SHLYDLSRSRSDKEKLHDEAVAICLDGQPLAMIQQLLLEVAVGLLNISTKDIVQSAIMKISALS
 GGSADLGGPRDPLKVLEGVVAAVHASVDKGEELVSPEDLLEWLRPFACDDAWPVRPRI
 HVLQILGQSFHLTEEDSKLLVFFRTEAILKASWPQRQVDIADIENEENRYCLFMELLESS
 HHETEFQHLVLLQAWPPMKSEYVITNNPWVRLATVMLTRCTMENKEGLGNEVLKMCR
 SLYNTKQMLPAEGVKELCLLNQSLLLPSLKLLLESRDEHLHEMALEQITAVTTVNDSN
 CDQELLSLLLDAKLLVKCVSTPFYPRIVDHLLASLQQGRWDAEELGRHLREAGHEAEAG
 SLLLAVRGTHQAFRTFSTALRAAQHWVLKPPVALLLSRKSIWS

SEQ ID No:147

RRMNHKSKKIREAKRSARPELKDSLWDTRHNYYESFSLSPIAVADNVERADALQLSV
 EEFVERYERPYKPVVLLNAQEGWSAQEKWTLERLKRKRNQKFCGEDNDGYSVKMK
 MKYYIEYMESTRDDSPLYIFDSSYGEHPKRRKLLEDYKVPKFTDDLFQYAGEKRRPPY
 RWFVMGPPRSGTGIIDPLGTSAWNALVQGHKRWCLFPTSTPRELIKVTRDEGGNQQ
 DEAITWFNVIYPRTQLPTWPPEFKPLEILQKPGETVFVPGGWWHVVLNLDTTIAITQNFA
 SSTNFPVVWHKTVRGRPKLSRKWYRILKQEHPPELAVLADSVDLQESTGIASDSSSDSSS
 SSSSSSSDSECESGSEGDTVHRRKKRRTCSMVGNGDTSQDDCVSKERSSSRIR
 DTCGGRAHP

SEQ ID No:148

MGSECVAGLSQTPQATLAANGAEDSRGGEMLPAGEIGASPAAPCCSESGDERKNLEE
 KSDINVTVLIGSKQVSEGTDNGDLPSYVSAFIEKEVGNDLKSLLDKLIEQRTVSKMQL
 EEQVLTISSEIPKRIRSALKNAEESKQFLNQFLEQETHLFSAINSHLLTAQPWMDDLGTMI
 SQIEEIERHLAYLKWIQSIEELSDNIQQYLMTNVPEAASTLVSMMAELDIKLQESSCTHLL
 GFMRATVKFWHKILKDKLTSDFEEILAQLHWPFIAPPQSQTVGSLRPASAPEIYSYLETL
 FCQLLKLQTSDELLTEPKQLPEKYSLPASPSVILPIQVMLTPLQKRFRYHFRGNRQTNVL
 SKPEWYLAQVLMWIGNHTEFLDEKIQPILDKVGSVLNARLEFSRGLMMLVLEKLATDIPC
 LLYDDNLFCHLVDEVLLFERELHSVHGYPGTFASCMHILSEETCFQRWLTVERKFALQK
 MDSMLSSEAAWSQYKDITDVDEMVKPDCAETFMTLLLVTDRYKNLPTASRKLQFLEL
 QKDLVDDFRIRLTQVMKEETRASLGFRYCAILNAVNYISTVLADWADNVFFLQLQQAALE
 VFAENNTLSKLQLGQLASMESSVFDDMINLLERLKHDMLTRQVDHVREVKDAAKLYKK
 ERWLSLPSQSEQAVMSLSSACPLLLTLRDHLLQLEQQLCFSLFKIFWQMLVEKLDVYIY
 QEIIILANHFNEGGAQLQFDMTRNLFPLFSHYCKRPNYFKHIKEACIVLNLNVGSALLK
 DVLQSASGQLSTTAALNEVGIYKLAQQDVEILLNLRTNWPNNTGK

SEQ ID No:149

MVLLTMIARVADGLPLAASMQEDEQSGRDLQQYQSQAQQLFRKLNEQS PTRCTLEAGA
 MTFHYIIEQGVCYVLCEAAFPKKLAFAYLEDLHSEFDEQHGKKVPTVSRPYSFIEDTFI
 QKTKKLYIDS RARRNLGSINTELQDVQRIMVANIEEVLQRGEALSALDSKANNLSSLSSKK
 YRQDAKYLNMRSTYAKLAAVAVFFIMLIVYVRFWWL

SEQ ID No:150

MSLEDPFFVVRGEVQKAVNTARGLYQRWCELLQESA AVGREELDWTTNELRNGLRSIE
 WDLEDLEETIGIVEANPGKFKLPAGDLQERKVVERMREAVQEMKDHMVSPTAVAFLE
 RNNREILAGKPAAQKSPSDL DASAVSATSRYIEEQQATQQLIMDEQDQQLEMVSGSIQ
 VLKHMSGRVGEELDEQGIMLDAFAQEMDHTQS RMDGVLRKLA KVSHMTSDRRQWC
 AVLGVVLLVLILLFSL

SEQ ID No:151

MAVDITLLFRASVKTVKTRNKALGVAVGGGVDGSRDEL FRRSPRPKGDFSSRAREVISH
 IGKL RDFLLEHRKDYINAY SHTMSEYGRMTDTERDQIDQDAQIFMRTCSEAIQQLRTEA
 HKEIHSQQVKEHRTAVLDFIEDYLKRVCKLYSEQRAIRVKRVVDKKRLSKLEPEPNTKTR
 ESTSSEKVSQSPSKDSEENPATEERPEKILAETQPELGTWGDKGEDELSPEEIQMFE

QENQRLIGEMNSLFDEVQRQIEGRVVEISRLQEIFTEKVLQQEAEIDSIHQLVVGATENIKE
GNEDIREAIKNNAAGFRVVILFFLVMCSFSLLFLDWYDS

SEQ ID No:152

MSCRDRTQEFLSACKSLQTRQNGIQTNKPALRAVRQRSEFTLMAKRIGKDLSNTFAKLE
KLTLAKRKSLFDDKAVEIEELTYIIKQDINSLNKQIAQLQDFVRAKGSQSGRHLQTHSNTI
VVSLQSKLASMSNDFKSVLEVRTENLKQQRSRREQFSRAPVSALPLAPNHGGAVVL
GAESHASKDVAIDMMDSRTSQQLQLIDEQDSYIQSRADTMQNIESTIVELGSIFQQLAHM
VKEQEETIQRIDENVLGAQLDVEAAHSEILKYFQSCTSQRWLMVKIFLILIVFFIIFVVFLA

SEQ ID No:153

MAAGTSSYWEDLRKQARQLENELDLKLVFSKLCSTSYSHSSTRDGRRDRYSSDTPL
NGSSQDRMFETMAIEIEQLLARLTGVNDKMAEYTNAGVPSLNAALMHTLQRHRDILQV
IYWARDVFIITGVVVVFFFNPICGYVHIYLKGQREKSEKINAMLKGLVLLFFGVTIJKF

SEQ ID No:154

MAGRSMQAARCPTDESLTNCSVVNEKDFQSGQHVIVRTSPNHRYTFTLKTHPSVPG
SIAFLPQRKWAGLSIGQEIEVSLYTDFDKAKQCIGMTIEIDFLQKKSNDSPYDTDKMAA
EFIQQFNNQAYSVGQQLVFSFNEKLFGLLVKDIESMDPSILKGEPATGKRQKIEVGLVVG
NSQVAFEKAENSSLNLIGKAKTKENRQSIIINPDWNFEKMGIGGLDKEFSDIFRRRAFAFRV
FPPEIVEQMGCIHVKGILLYGPPCGKTLLARQIGKMLNAREPKVVNGPEILNKYVGSE
ANIRKLFADAEEEQRRRLGANSGLIIIIFDEIDAICKQRGSMAGSTGVHDTVNVQQLSKIDG
VEQLNNILVIGMTNRPDLIDEALLRPGRLEVKMEIGLPDEKGRQLQILHIHTARMRGHQLLS
ADVDIKELAVETKNFGSAELEGIVRAAQSTAMNRHIKASTKVEVDMEKAESLQVTRGDF
LASLENDIKPAFGTNQEDYASYIMNGIICKWGDPVTRVLDGELLVQQTKNSDRTPLVSVL
LEGPPHSGKTALAIAEESNFPFIKICSPDKMIGFSETAKCQAMKKIFDDAYKSQLSCVV
VDDIERLLDYVPIGPRFSNLVLQALLVLLKKAPPQGRKLLIIGTSRKDVLQEMEMLNAFS
TTIHVPNIATGEQLLEALELLGNLKDERTTIAQQVKGKKWIGIKKLLMLIEMSLQMDPE
YRVRKFLALLREEGASPLDFD

SEQ ID No:155

MAGGRTAAAASIRERQTVALKRMLNFNVPHIKNSTGEPVWKVLIYDRFGQDIISPLLSV
KELRDMGITLHLLLHSDRDPIDPVPAVYFVMPTEENIDRMCQDLRNQLYESYYLNFISAIS
RSKLEDIANAALELSAVTQVAKVFDQYLNFITLEDDMFVLCNQNKEVSYRAINRPDITDT

EMETVMDTIVDSLFCFYGTLGAVPIIRCSRGTAAEMVAVKLDKKLRENLRDARNSLFTG
 DTLGAGQFSFQRPLLVLVDRNIDLATPLHHTWTYQALVHDVLFHLNRVNLEESSGVEN
 SPAGARPKRKNKSYDLTPVDKFQKHKGSPFPEVAESVQQELESYRAQEDEVKRLK
 SIMGLEGEDEGAISMLSNTAKLTSAVSSLPELLEKKRLIDLHTNVATAVLEHIKARKLDV
 YFEYEKIMSKTLDKSLLDIISDPDAGTPEDKMRLFLIYYISTQQAPSEADLEQYKKALT
 DAEMNLNPLQYIKQWKAFTKMASAPASYGSTTKPMGLLSRVMNTGSQFVMEGVKNL
 VLKQQNLPVTRILDNLMEMKSNPKDDYRYFDPKMLRGNDSSVPRNKNPFQEAIVFVV
 GGGNYIEYQNLVDYIKGKQGKHILYGCSELFNATQFIKQLSQLGQK

SEQ ID No:156

MSFLIDSSIMITSQLFFFGFWLFFMRQLFKDYEIRQYVVQVIFSVTFAFSCTMFELIIFEIL
 GVLNSSSRYFHWKMNLCVILLILVFMVPFYIGYFIVSNIRLLHKQRLLFSCLLWLTMYFF
 WKLGDPFPILSPKHGILSIEQLISRVGIVGVTLMALLSGFGAVNCPTYMSYFLRNVTDTD
 ILALERRLLQTMDMIISKKRMAMARRTMFQKGEVHNKPMSGFWGMIKSVTTSASGSENL
 TLIQQEVDALEELSRQLFLETADLYATKERIEYSKTFKGKYFNFLGYFFSIYCVWKIFMATI
 NIVFDRVGVKTDPVTRGIEITVNYLGIQFDVKFWSQHISFILVGIIIVTSIRGLLTLKFFYAI
 SSKSSNVIVLLAQIMGMYFVSSVLLIRMSMPLYRTIITEVLGELQFNFYHRWFDVIFLVS
 ALSSILFLYLAHKQAPEKQMAP

SEQ ID No:157

MRSPATGVPLPTPPPLLLLLLPPPLLGDQVGPCRSLGSRGRRGSSGACAPMGWLC
 PSSASNLWLYTSRCRDAGTELGTGHLPVPHDGLRVWCPSEAHIPPAPEGCPWSCR
 LLGIGGHLSPQGKLTLPEEHPCLKAPRLRCQSCCKLAQAPGLRAGERSPEESLGRRKR
 NVNTAPQFQPPSYQATVPENQPAGTPVASLRAIDPDEGEAGRLEYTMDALFDSRSNQF
 FSLDPVTGAVTAEELDRETKSTHVFRVTAQDHGMPRRSALATLILVTDNDHDPVFE
 QQEYKESLRENLEVGYEVLTVRATDGDAPPANILYRLLEGSGGSPSEVFEIDPRSGVI
 RTRGPVDREEVESYQLTVEASDQGRDPGPRSTTAAVFLSVEDDNDNAPQFSEKRYVV
 QVREDVTPGAPVLRVTASDRDKGSNAVHYSIMSGNARGQFYLDAQTGALDVVSPLDY
 ETTKEYTLRVRAQDGGRPPLSNVGLTVQVLDINDNAPIFVSTPFQATVLESVPLGYLV
 LHVQAIADAGDNARLEYRLAGVGHDFFTIINNGTGWISVAAELDREEVDFYSFGVEAR
 DHGTPALTASASVSVTVLDVNDNNPTFTQPEYTVRLNEDAAGTSVTVSAVDRDAHS
 VITYQITSGNTRNRFSITSQSGGGLVSLALPLDYKLERQYVLAVTASDGTRQDTAQIVVN
 VTDANTHRPVFQSSHYTNVNEDRPAGTTVVLISATDEDTGENARITYFMEDSIPQFRID
 ADTGAVTTQAELDYEDQVSYTLAITARDNGIPQKSDTTLLEILVNDVNDNAPQFLRDSYQ

GSVYEDVPPFTSVLQISATDRDSGLNGRVFYTQGGDDGDFIVESTSGIVRTLRLD
 RENVAQYVLRAYAVDKGMPPARTPMEVTVLDVNDNPPVFEQDEFDVVEENSPIGL
 AVARVTATDPDEGTNAQIMYQIVEGNIPEVFQLDIFSGELTALVDLDYEDRPEYVLVIQAT
 SAPLVS RATVHVRLDRNDNPPV LGNFEILFNNYVTNRSSFP GGAIGR VPAHD PDISD
 SLTYSFERGNELSLVLLNASTGELKLSRALDNNRPLEAIMSVLVSDGVHSVTAQC ALRVT
 IITDEM LTHSITLRLEDMSPERFLSP LLGLFIQAVAATLATPPDHVVVFNVQR DTDAPGGH
 ILNVSLSVGQPPGP GGGPPFLP SEDLQERLYLNRSLLTAISAQRVLPFDDN ICLREPCEN
 YMRCVSVLRFDSSAPFIASSSVLFRPIHPV GGLRCRCPPGFTGDYCETEVDLCYSRPCG
 PHGRCRSREGGYTCLCRDGYTGEHCEVSARSGRCTPGVCKNGGTCVNLLVGGFKCD
 CPSGD F EKPYCQV TTRSF PAHS FITFRGLRQRFHFTLALSFA TKERDG LLYNGRFNEK
 HDFVALEVIQE QVQLTFSAGE STT VSPFVPGG VSDGQWHTVQLKYYNKPLL GQTGLP
 QGPSEQKVAVVTVDGCDTGVALRG SVLG NYSCAAQGTQGGSKS LDTGPLLGGV
 PDLPESFPVRMRQFVGCMRNLQVDSRHIDMADFIANNGTVPGCPAKKNV CDSNTCHN
 GGTCVNQWDAFSC ECPLGF GGKSCAQEMANPQHFLGSSLVAHGLSLPISQPWYLSL
 MFRTRQADGVLLQAITRGRSTITLQLREGHVMLSVEGTGLQASSLRLEPGRANDGDWH
 HAQLALGASGGPGHAILSFDYQQRAEGNLGPR LHGLHLSNITVGGIPGPAGGVARGF
 RGCLQGV RVSDTPEGVNSLDPSHGESINVEQGCSLPDCSNPCPANSYCSNDWDSY
 SCSCDPGYYGDNCTNVCDLN PCEHQSVCTR KPSAPHGYTCECPPNYLG PYCETRIDQ
 PCPRGWWGHPTCGPCNC DVSKGFDPDCNKTSGE CHCKENHYRPPGSPTCLLCDCYP
 TGSLSRVCDPEDGQCPCKPGVIGRQCDRC DNPF AEVTTNGCEVNYDSCPRAIEAGIW
 WPRTRFGLPAAAPCPKG SFGTAVRHCDEHRGWLPNLFNCTSITFSELKGFAERLQRN
 ESGLDSGRSQQLALLRNATQHTAGYFGSDVKVAYQLATRLLAHESTQRGFGLSATQD
 VHFTENLLRVGSALLDTANKRHWE LIQQTEGGTAWLLQHYEAYASALAQNMRHTYLSP
 FTIVTPNIVISVVR LDKG NFAGAKLPRYEALRGEQPPDLETTVILPESVFR ETPVVRPAG
 PGEAQEPEELARRQRRHPELSQGEAVASVIIYRTL AGLLPHNYDPDKRSLRVPKRPIINT
 PVVSISVHDDEELLPRALDKPVTVQFRLLET EERTKPICVFWNHSILVSGTGGWSARGC
 EVVFRNESHVSCQCNHMTSFAVLM DVSRR ENGEILPLKLT YVALGVTLA ALLLTFFF LT
 LLRILRSNQHGIRRNLT AALGLAQLVFL LGINQADLPFACTVIAILLHFLYLC TFSW ALLEAL
 HLYRALTEVRDVNTGPMRFYYMLGWGVPAFITGLAVGLDPEGYGNPDFCWLSIYDTLI
 WSFAGPVAFAVSMSVFLYILAARASCAAQRQGF EKKGPVSGLQPSFAVLLLSATWLLA
 LLSVNSDTLLFH YLFATCNCI QGPFI LS YVVL SKEVRKALKLACSRKPSPDPALT KSTL
 TSSYNCSPYADGR LYQPYGDSAGSLHSTS RSGKS QPSYIPFLL REESALNPGQGPPG
 LGDPGSLFLEGQDQQHDPDTDS DSDLSLEDDQSGSYASTHSSDSEEEEEEEA AF
 PGEQGWDSLLGPG AERLPLHSTPKDGGPGPGKAPWPGDFGTTAKESSGNGAPEERL

RENGDALSREGSLGPLGSSAQPHKGILKKKCLPTISEKSSLRLPLEQCTGSSRGSSA
SEGSRGGPPPRPPPRQLQEQLNGVMPIAMSIKAGTVDEDSSGSEFLFFNFLH

SEQ ID No:158

MLRRPAPALAPAARLLLALLCGGGVWAARVNKHKPWLEPTYHGIVTENDNTVLLDPP
LIALDKDAPLRFAESFEVTKEGEICGFKIHGQNVPFDAVVVDKSTGEGVIRSKEKLDC
ELQKDYSFTIQAYDCGKGPDGTNVKKSHKATVHIQVNDVNEYAPVFKEKSYKATVIEGK
QYDSILRVEAVDADCSPQFSQICSYEIITPDVPFTVDKDGYIKNTEKLYGKEHQYKLTVT
AYDCGKKRATEDVLVKISIKPTCTPGWQGWNNRIEYEPGTGALAVFPNIHLETCDPVA
SVQATVELETSHIGKGCDRTYSEKSLHRLCGAAAGTAELLPSPSGSLNWTMGLPTDN
GHDSDQVFEFNGTQAVERIPDGVVSPKEPFTISVWMRHPGRKKETILCSSDKTDM
NRHHYSLYVHGCRLLFRQDPSEEKKYRPAEFHWKLNQVCDEEWHHYVLNVEFPSVT
LYVDGTSHEPFSTEDYPLHPSKIETQLVVGACWQEFSGVENDNETEPVTVASAGGDL
HMTQFFRGNLAGLTLRSGKLADKKVIDCLYTCKEGLDLQVLEDSGRGVQIQAHPSQLVL
TLEGEDLGELDKAMQHISYLNRSRQFPTPGIRRLKITSTIKCFNEATCISVPPVDGYVMVLQ
PEEPKISLSGVHHFARAASEFESSEGVFVLFPELRIISTITREVEPEGDGAEDPTVQESLVS
EEIVHDLDTCEVTVEGEELNHEQESLEVDMARLQQKGIEVSSSELGMTFTGVDTMASY
EEVLHLLRYRNWHARSLLDRKFKLICSELNGRYISNEFKVEVNVVIHTANPMEHANHMAA
QPQFVHPEHRSFVDLSGHNLANPHPFAVVPSTATVVIVVCSVFLVFMIIILGVFRIRAAHR
RTMRDQDTGKENEMDWDDSAITITVNPMETYEDQHSSEEEEEEESEDGEEDD
ITSAESESSEEEGEQGDPQNATTRQQQLEWDDSTLSY

SEQ ID No:159

MGKGGNQGEGAAEREVSVPTFSWEIQQKHNLRDRLVIDRKVYNITKWSIQHPGGQ
RVIGHYAGEDATDAFRAFHLDLEFGKFLKPLLIGELAPEEPSQDHGKNSKITEDFRALR
KTAEDMNLFKTNHVFFLLLAHIIALESIAWFTVFYFGNGWIPTLITAFVLATSQAQAGWL
QHDYGHLSVYRKPKWNHLVHKFVIGHLKASANWWNHRHFQHHAKPNIFHKDPDVNM
LHVFLGEWQPIEYGKKKLKYLPYNHQHEYFFLIGPPLLIPMYFQYQIIMTMIVHKNWDL
AWAVSYYIRFFITYIPFYGILGALLFLNFIRFLESHWFVVVTQMNHIVMEIDQEAYRDWFS
SQLTATCNVEQSFFNDWFSGHLNFQIEHHLFPTMPRHNLHKIAPLVKSLCAKHGIEYQE
KPLLRALLDIIRSLKKSGKLWLDAYLHK

SEQ ID No:160

MTATEALLRVLLLLAFGHSTYGAECFPACNPQNGFCEDDNVCRCQPGWQGPLCDQC
 VTSPGCLHGLCCEPGQCICTDGWDGECLRDVRACSSAPCANNGTCVSLGGLYECS
 CAPGYSGKDCQKKDGPCVINGSPCQHGGTCVDDEGRASHASCLCPPGFSGNFCEIVA
 NSCTPNPCENDGVCTDIGGDFRCRCPAGFIDKTCSRPVNCASSPCQNNGTCLQHTQ
 VSYECLCKPEFTGLTCVKKRALSPQQVTRLPSGYGLAYRLTPVHELPVQQPEHRILKV
 SMKELNKKTPLLTEGQAICFTILGVLTSLVVLGTVGIVFLNKETWVSNLRYNHMLRKKK
 NLLLQYNNSGEDLAVNIIFPEKIDMTTSKEAGDEEI

SEQ ID No:161

MELHYLAKKSQNADLCDARDWSSRGLPGDQADTAATRAALCCQKQCASTPRATEME
 GSKLSSSPASPSSLQNSTLQPDAFPPGLLHSGNNQITAERKVCNCCSQELETSFTYVD
 KNINLEQRNRSSPSAKGHNHPGELGWENPNEWSQEAAISLISEEEEDTSSEATSSGKSI
 DYGFISAILFLVTGILLVIISYIVPREVTVDPTVAAREMERLEKESARLGAHLDRCVIAGLC
 LLTLGGVILSCLLMMSMWKGELYRRNRFASSKESAKLYGSFNFRMKTSTNENTLELSV
 EEDALAVQS

SEQ ID No:162

MAPRPLGPLVLALGAAAVLGSVLFILWKTYFGRGRERRWDRGEAWWGAEARLPE
 WDEWDPEDEEDEEPALLEEQREVLVLGLDGAGKSTFLRVLSGKPPLLEGHIPTWGFNS
 VRLPTKDFEVDLLEIGGSQNLRFYWKEFVSEVDVLVFVVDSADRRLRPWARQELHKLLD
 KDPDLPVVVVANKQDLSEAMSMGELQRELGLQAIDNQREVFLAASIAPAGPTFEEPGT
 VHIWKLLLELLS

SEQ ID No:163

MSDSGSQLGSMGSLTMKSQLQITVISAKLKENKKNWFGPSPYVEVTVDGQSKKTECN
 NTNSPKWKQPLTVIPTVSKLHFRTVSHQTLKSDVLLGTAALDIYETLKSNNMKLEEVV
 VTLQLGGDKEPTETIGDLSICLDGLQLESEVVNTGETCSENGVSLCLPRLECNSAISAH
 CNLCLPGLSDSPISASRVAGFTGASQNDGSRSKDETRVSTNGSDDPEDAGAGENRR
 VSGNNSPSLSNGGFKPSRPPRPSRPPPPTPRRPASVNGSPSATSESDGSSTGSLPPT
 NTNTNTSEGATSGLIPLTISGGSGPRPLNPVTQAPLPPGWEQRVDQHGRVYYVDHVEK
 RTTWDRPEPLPPGWERRVDNMGRYYDHFTRTTWQRPTLESVRNYEQWQLQRSQ
 LQGAMQQFNQRFIYGNQDLFATSQSKEFDPLGPLPPGWEKRTDSNGRVYFVNHNTRIT
 QWEDPRSQGQLNEKPLPEGWEMRFTVDGIPYFVDHNRRTTTIDPRTGKSALDNGPQI
 AYVRDFKAKVQYFRFWCQQLAMPQHIKITVTRKTLFEDSFQQIMSFSPQDLRRRLWVIF

PGEEGLDYGGVAREWFFLLSHEVLNPMLYCLFEYAGKDNYCLQINPASYINPDHLKYFRF
IGRFIAMALFHGKFIDTGFSLPFYKRILNPKVGLKDLESIDPEFYNSLIWVKENNIEECDEL
MYFSVDKEILGEIKSHDLKPNNGNIVTEENKEEYIRMVAEWRLSRGVVEEQTQAFFEGF
NEILPQQYLQYFDAKELEVLLCGMQEIDLNDWQRHAIYRHYARTSKQIMWFQFVKEID
NEKRMRLLQFVTGTCRGPVGGFADLMGSNGPQKFCIEKVGKENWLPRSHTCFNRLDL
PPYKSYEQLKEKLLFAIEETEGFGQE

SEQ ID No:164

LQLSVKMSVLISQSVINYVEEENIPALKALLEKCKDVDERNECGQTPLMIAAEQGNLEIVK
ELIKNGANCNLEDLDNWTLISASKEGHVHIVEELLKCGVNLEHRDMGGWTALMWACY
KGRTDVVELLSHGANPSVTGLYSVYPIWAAGRGHADIVHLLLQNGAKVNCSDKYGT
PLVWAARKGHLECVKHLLAMGADVQEGANSMTALIVAVKGGYTQSVKEILKRNPNVN
LTDKGNTALMIASKEGHTEIVQDLLDAGTYVNIPDRSGDTVLIGAVRGGHVEIVRALLQ
KYADIDIRGQDNKTALYWAVEKGNATVRDILQCNPDTETCKDGETPLIKATKMRNIEV
VELLLDKGAKVSAVDKKGDTPLHIAIRGRSRKLAELLRNPKDGRLLYRPNKAGETPYNI
DCSHQKSILTQIFGARHLSPTETDGDMLYDLYSSALADILSEPTMQPPICVGLYAQWG
SGKSFLKKLEDEMKTFAQQQIEPLFQFSWLIVFLTLLCGGLGLLFAFTVHPNLGIAVSL
SFLALLYIFFIVIYFGGRREGESWNWAWSLSTRLARHIGYLELLLKLMFVNPPPEQTTK
ALPVRFLFTDYNRLSSVGGETS LAEMIATLSDACEREFGFLATRLFRVFKTEDTQGKKK
WKKTCCLPSFVIFLFIIGCIISGITLLAIFRVDPKHLTVNAVLISIASVVGGLAFVLCRTWWQ
VLDSSLNSQRKRLHNAASKLHKLKSEGMKVLKCEVELMARMAKTIDSFTQNQTRLVII
DGLDACEQDKVLQMLDTVRLFSKGPFIAIFASDPHIKKAINQNLNSVLRDSNINGHDYM
RNIVHLPVFLNSRGLSNARKFLVTSATNGDVPCSDTTGIQEDADRRVSQNSLGEMTKLG
SKTALNRRDTYRRRQMQRITRQMSFDLTKLVTEDWFSDISPQTMRRLLNIVSVTGR
LRANQISFNWDRLASWINLTEQWPYRTSWLILYLEETEGIPDQMTLKIYERISKNIPTTK
DVEPLLEIDGDIRNFEVFLSSRTPVLVARDVKVFLPCTVNLDPLKREIIADVRAAREQISIG
GLAYPPLPLHEGPPRAPSGYSQPPSVCSSTSNGPFAGGVVSPQPHSSYYSGMTGPQ
HPFYNRPFFAPYLYTPRYYPGGSQHLISRPSVKTSLPRDQNNGLEVIKEDAAEGLSSPT
DSSRGSGPAPGPVVLLNSLNDAVCEKLKQIEGLDQSMLPQYCTTIKKANINGRVLAC
NIDELKKEMNMNFGDWHLFRSTVLEMRNAESHVVPEDPRFLSESSSGPAPHGEPAR
ASHNELPHTELSSQTPYTLNFSFEELNTLGLDEGAPRHSNLSWQSQTRRTPSLSSLNS
QDSSIEISKLTDKVQAERYDAYREYIAQMSQLEGGPGSTTISGRSSPHSTYYMGQSSSG
GSIHSNLEQEKGKDSEPKPDDGRKSFLMKRGDVIDYSSSGVSTNDASPLDPITEEDEKS
DQSGSKLLPGKKSSERSSLFQTDLKLKGSLRYQKLPSDEDESGTEESDNTPLLKDDK

DRKAEGKVERVPKSPEHSAEPIRTFIKAKEYLSDALLDKDSSDSGVRSSESSPNHSLH
 NEVADDSQLEKANLIELEDDSHSGKRGIPHSGLQDPIIARMSICSEDKKSPSECSCLIAS
 SPEENWPACQKAYNLNRTPSTVTLNNSAPANRANQFDEMEGIRETSQVILRPSSSP
 NPTTIQNENLKSMTHKRSQRSSYTRLSKDPPELHAAASSESTGFGEERESIL

SEQ ID No:165

MATAGGGSGADPGSRGLLRLSFCVLLAGLCRGNNSVERKIYIPLNKTAPCVRLLNATHQI
 GCQSSISGDTGVIHVVEKEEDLQWVLTDPNPYMLLESKHFTRDLMEKLKGRTSRIA
 GLAVSLTKPSPASGFSPSVQCPNDGFGVYSNSYGPEFAHCRCIQWNNSLGNGLAYEDFS
 FPIFLLEDENETKVIKQCYQDHNLSQNGSAPTFFPLCAMQLFSHMHAVISTATCMRRSSIQ
 STFSINPEIVCDPLSDYNVWSMLKPINTTGTLPDDRVVVAATRLDSRSFFWNVAPGAE
 SAVASFVTQLAAAEEALQKAPDVTLPRNVMFVFFQGETFDYIGSSRMVYDMEKGKFPV
 QLENVDSFVELGQVALRTSLELWMHTDPVSQKNESVRNQVEDLLATLEKSGAGVPAVI
 LRRPNQSQPLPPSSLQRFLRARNISGVVLADHSGAFHNKYYQSIYDTAENINVSYPEWL
 SPEEDLFNTDTAKALADVATVLGRALYELAGGTNFSDTVQADPQTVTRLLYGFLIKAN
 NSWFQSILRQDLRSYLGDPQLQHYIAVSSPTNTTYVVQYALANLTGTVVNLTREQCQDP
 SKVPSENKDLYEYSWVQGPLHSNETDRLPRCVRSTARLARALSPAELSQWSSTEYST
 WTESRWKDIRARIFLIASKELELITLTVGFGILIFSLIVTYCINAKADVLFIAPREPGAVSY

SEQ ID No:166

MEDLDQSPLVSSSDSPPRPQPAFKYQFVREPEDEEEEEEEEEEDEDLEELEVLERK
 PAAGLSAAPVPTAPAAGAPLMDFGNDVPPAPRGPLAPPVAPERQPSWDPSPVSS
 TVPAPSPLSAAAVSPSKLPEDDEPPARPPPPPASVSPQAEPVWTPPAPAPAAPPSTP
 AAPKRRGSSGSVDETLFALPAASEPVISSAENMDLKEQPGNTISAGQEDFPSVLLETA
 ASLPSLSPLSAASFKEHEYLGNLSTVLTEGTLQENVSEASKEVSEAKTLLIDRDLTEF
 SELEYSEMGSFSVSPKAESA VIVANPREEIIVKNKDEEEKLVSNNILHNQQELPTALT
 VKEDEVVSSEKAKDSFNEKRVAVEAPMREEYADFKPFERVWEVKDSKEDSDMLAAGG
 KIESNLESKVDKCFADSLEQTNHEKDSESSNDDSFSTPEGIKDRSGAYITCAPFNPA
 ATESIATNIFPLLGDPSENKTDEKKIEEKKAQIVTEKNTSTKTSNPFLVAAQDSETDYVT
 TDNLTKVTEEVVANMPEGLTPDLVQEACESELNEVTGKIA YETKMDLVQTSEVMQESL
 YPAAQLCPSEEESEATPSVLPDIVMEAPLNSAVPSAGASVIQPSSS PLEASSVYESIK
 HEPENPPPYEEAMS VSLKKVSGIKEEIKE PENINA ALQETEAPYISIACDLIKETKLSAEPA
 PDFSDYSEMAKVEQPVPDHSELVEDSSPDSEPVDFLSDD SIPDVPQKQDETVMLVKES
 LTETSFESMIEYENKEKLSALPPEGGKPYLESFKLSDLNTKDTLLPDEVSTLSKKEIPLQ

MEELSTAVYSNDDLFIKEAQIRETETFSDSSPIEIIDEFPTLISSKTDIFSKLAREYTDLEV
 SHKSEIANAPDGAGSLPCTELPHDLSLKNIQPKVEEKISFSDDFSKNGSATSKVLLPPD
 VSALATQAEIESIVKPKVLVKEAEKKLPSTDTEKEDRSPSAIFSAELSCTSVDLLYWRDIK
 KTGVVFgaslfllsLTvFsIVSVTAYIALALLSVTISFRIYKGVIQAIQKSDEGHPFRAYLE
 SEVAISEELVQKYSNSALGHVNCTIKELRRFLVDDLVDSLKFAVLMWVFTYVGALFNGL
 TLLILALISLFSVPVIYERHQAQIDHYLGLANKNVKDAMAKIQAKIPGLKRKAE

SEQ ID No:167

MRLPGAMPALALKGELLLLSLLLLLEPQISQGLVVTPPGPELVNVSSTFVLTCSGSAPV
 VWERMSQEPPQEMAKAQDGTSSVLTNTGLDTGEYFCTHNDSRGLETDERKRLYI
 FVPDPTVGFLPNDAEELFIFLTIEITIPCRVTDPQLVVTLHEKKGDVALPVPYDHQRGF
 SGIFEDRSYICKTTIGDREVDSDAYYVYRLQVSSINVSNAVQTVVVRQGENITLMCIVIGN
 EVVNFEWTYPRKESGRIVEPVTDFLLDMPYHIRSILHIPS A ELED SGTYTCNVTESVNDH
 QDEKAINITVVESGYVRLLGEVGTQLQFAELHRSRTLQVVFEAYPPPTVLWFKDNRG
 SSAGEIALSTRNVSETRYVSELTLRVVKVAEAGHYTMRAFHEDAEVQLSFQLQINV
 VPR VLELSESHPDSGEQTVRCRGMPQPNIWSACRDLKRCPRELPPTLLGNSSEEESQL
 ETNVTYWEEEQEFEVVSTLRLQHVDRPLSVRCTLRNAVGQDTQEVI
 VPHSLPFKV
 VVVI SAILALVVLTIISLIIIMLWQKKPRYEIRWKVIESVSSDGHEYIYV
 DPMQLPYDSTWELPR
 DQLVLRGRTLGSGAFGQVVEATAHGLSHSQATMKVAVKMLKSTAR
 SSEKQALMSELKIM
 SHLGPHLNVVNLLGACTKGGPIYIITEYCRYGDLVDYLHRNKHTFLQHHSDKRRPPSAEL
 YSNALPVGLPLPSHVS LTGESDGGYMDMSKDESVDYVPM
 LDMKGDVKYADI
 ESSNYM
 APYDNYVPSA
 PERTCRATLINESPVLSYMDLVGF SYQVANGMEFLASKNCV
 HRDLAAR
 NVLICEGKLVKICDFGLARDIMRDSNYISKGSTFLPLKWM
 APESIFNSLY
 TTLSDVWSFGI
 LLWEIFTLGGTPYPELPMNEQFYNAIKRGYRMAQPAHASDEIYE
 IMQKC
 WEEKFEIRPP
 FSQ
 LVLLLERLLGEGYKKYQQVDEEFLRSDHP
 AILRSQARLPGFHGLRSPLDTSSVLY
 TAVQPNEGNDYI
 IIPDPKPEVADEGPLEGSPSLASSTLNEVNTS
 STISCDSP
 LEHQDE
 PEPEPQLELQVEPEPELEQLPD
 SGCPAPRAEAEDSFL

SEQ ID No:168

MGAARGSPARPRLPLLSVLLLPLLGGTQTAIVFIKQPSSQDALQGRRALLRCE
 VEAPG
 PVHVYWLLDGAPVQDTERRFAQGSSLSFAAVDPLQDSGTFQC
 VARDDVTGE
 EARSAN
 ASFN
 IKWIEAGPVVLKHP
 ASEAEIQPQTQVKLRCHIDGH
 PRPTYQWFRDGTPLSDGQSN
 HTVSSKERNLTLRPAGPEHSGLYSCCAHS
 AFSSQACSSQNFTLSIA
 DESFARVVLAPQDV
 VVARYEEAMFH
 CQFSAQPPPSLQWL
 FEDETPTINRSRPPHLRRATV
 FANGSLLTQVR

PRNAGIYRCIGQQQRGPPPIILEATLHLAEIEDMPLFEPRVFTAGSEERVTCCLPPKGLPEPS
 VVWEHAGVRLPTHGRVYQKGHELVLANIAESDAGVYTCHAANLAGQRRQDVNITVAT
 VPSWLKKPQDSQLEEGKPGYLDCLTQATPKPTVVWYRNQMLISEDSRFEVKNGTLRI
 NSVEVYDGTWYRCMSSTPAGSIEAQAVLQVLEKLKFTPPPQPQQCMGFDKEATVPCS
 ATGREKPTIKWERADGSSLPEWVTDNAGTLHFARVTRDDAGNYTCIASNGPQGGQIRAH
 VQLTVAVFITFKVEPERTTVYQGHTALLQCEAQGDPKPLIQWKKGKDRILDPTKLGPRMHI
 FQNGSLVIHDVAPEDSGRYTCIAGNSCNIKHTEAPLYVVDKPVPEESEGPGSPPPYKMI
 QTIGLSVGAAVAYIIAVGLMFYCKKRCKAKRLQKQPEGEEPEMECLNGGPLQNGQPS
 AEIQEEVALTSLGSGPAATNKRHSTSDFMHFPRSSLQPIITLGKSEFGEVFLAKAQGLE
 EGVAETLVLVKSLSQSKDEQQQLDFRRELEMFGKLNHANVVRLGLCREAEPHYMVLEY
 VDLEDLKQFLRISKSKDEKLKSQPLSTKQKVALCTQVALGMELHSNNRFVHKDLAARN
 LVSAQRQVKVSALGLSKDVYNSEYYHFRQAWVALRWMSPEAILEGDFSTKSDWASG
 VLMWEVFTHGEMPHGGQADDEVLAIDLQAGKARLPQPEGCPSKLYRLMQRCWALSPK
 DRPSFSEIASALGDSTVDSKP

SEQ ID No:169

MPSSVSWGILLLAGLCCLVPVSLAEDPQGDAAQKTDTSHHDDQDHPTFNKITPNLAEFAF
 SLYRQLAHQSNSTNIFSPVSIATAFAMILSLGKADTHDEILEGLNFNLTEIPEAQIHEGF
 QELLRTLNQPDSQLQLTTGNGLFLSEGLKLVDFKLEDVKKLYHSEAFTVNFGDTEEAKK
 QINDYVEKGTQGKIVDLVKELDRDTVFALVNYIFFKGKWERPFEVKDTEEEDFHVDQVT
 TVKVPMMKRLGMFNIQHCKKLSSWVLLMKYLGNAATAIFFLPDEGKLQHLENELTHDIITK
 FLENEDRRSASLHLPKLSITGYDLKSVLGQLGITKVFSNGADLSGVTEEAPLKLASKAVH
 KAVLTIDEKGTEAAGAMFLEAIPMSIPPEVKFNKPFVFLMIEQNTKSPLFMGKVVNPQTQK

SEQ ID No:170

MVSIPEYYEGKNVLLTGTGFLGKVLLEKLLRSCPKVNSVYVLVRQKAGQTPQERVEEV
 LSGKLFDRLRDENPDFREKIIAINSELTKPLALSEEDKEVIDSTNIIFHCAATVRFNENLR
 DAVQLNVIATRQLILLAQQMKNLEVFMHVSTAYAYCNRKHIDEVVYPPPVDPKKLIDSLE
 WMDDGLVNDITPKLIGDRPNTIYTKALAELYVQQEGAELNVAIVRPSIVGASWKEPFPG
 WIDNFNGPSGLFIAAGKGILRTIRASNNAADLVPVDVVVMSAAAWYSGVNRPRNIM
 VYNCTTGSTNPFWGEVEYHVISTFKRNPLEQAFFRPNVNLTSNHLLYHYWIAVSHKAP
 AFLYDIYLRMTGRSPRCPSFKNSNSLSSHYRKGVSHRVSALLDCTHVRSETATFNI
 DVRQLHWA耶IENYCLGKYYVLNEEMSGLPAARKHLNKTLSLFHTALCHGKLT
 TFGFPCLLASGGPLLSVSLHFSAYVYSQIHLAFILRDLSHSAPS LASLAGPRELTVGSLL

DREWRQIKTDDFELGSAGEVDLEGADIEGCLLATSPA VRQQALLQRGVQWYISIPTTQ
ETVAMEMQI

SEQ ID No:171

MATRSSRRESRLPFLFTLVALLPPGALCEVWTQRLHGGSAPLPQDRGFLVVQGDPREL
RLWARGDARGASRADEKPLRRRSAALQPEPIKVYGQVSLNDSHNQMVVHWAGEKS
NVIVALARDSLALARPKSSDVYVSYDYGKSFKKISDKLNFGLGNRSEAVIAQFYHSPADN
KRYIFADAYAQYLWITFDFCNTLQGFSIPFRAADLLLHSKASNLLGFDRSHPNKQLWKS
DDFGQTWIMIQEHVKSFSWGIDPYDKPNTIYIERHEPSGYSTVFRSTDFFQSRENQEVL
EEVRDFQLRDKYMFATKVVHLLGSEQQQSSVQLWVSFGRKPMRAAQFVTRHPINEYYIA
DASEDQVFVCVSHSNNRTNLYISEAEGLKFSLSLENVLYSPGGAGSDTLVRYFANEPEF
ADFHRVEGLQGVYIATLINGSMNEENMRSVITFDKGHTWEFLQAPAFTGYGEKINCELS
QGCSLHLAQRLSQLLNQLRRMPILSKESAPGLIATGSVGKNLASKTNVYISSSAGARW
REALPGPHYYTWGDHGGIITAIAQGMETNELKYSTNEGETWKTIFSEKPVFVYGLTEP
GEKSTVFTIFGSNKENVHSWLILQVNATDALGPCTENDYKLWSPSDERGNECLLGHK
TVFKRRTPHATCFNGEDFDRPVVVSNCSCREDYECDFGFKMSEDLSLEVCPDPEFS
GKSYSPPVPCPGYSTYRRTRGYRKISGDTCSGGDVEARLEGELVPCPLAEEENEFLYAV
RKSIIYRYDLASGATEQLPLTGLRAAVALDFDYEHNCYLWSDLALDVIQRLCLNGSTGQE
VIINSGLETVEALAFEPLSQLLYWVDAGFKKIEVANPDGDFRLTIVNSSVLDPRRALVLVP
QEGVMFWTDWGDLKPGIYRSNMDGSAAYHLVSEDVWPNGISVDDQWIYWTDAYLE
CIERITFSGQQRSVILDNLPHPYAIAVFKNEIYWDDWSQLSIFRASKYSGSQMEILANQLT
GLMDMKIFYKGKNTGSACVPRPCSLLCLPKANNSRSCRCPEDVSSVLPMSGDLMCD
CPQGYQLKNNTCVKEENTCLRNQYRCNSNGNCINSIWWDNFQCRNGHCIPQRWACDGDTDCQDGS
CDLDTQFRCQESGTICPLSYKCDLEDDCGDNSDESHCEMHQCRSDEYNCSSGMCIRS
SWVCDGDNDCRDWSDEANCTAIYHTCEASFQCRNGHCIPQRWACDGDTDCQDGS
DEDPVNCEKKCNGFRCPNGTCIPSSKHCDGLRDCSDGSDEQHCEPLCTHFMDFVCKN
RQQCLFHSMVCDGIIQCRDGSDEAAFAGCSQDPEFHVCDEFGFQCQNGVCISLIWK
CDGMDDCGDYSDEANCENPTEAPNCSRYFQFRCENGHCIPNRWKCDRENDGDWS
DEKDCGDSHILPFSTPGPSTCLPNYYRCSSGTCVMDTWCDGYRDCADGSDEEACPL
LANVTAASTPTQLGRCDRFEFECHQPKTCIPNWKRCDGHQDCQDGRDEANCPTHSTL
TCMSREFQCEDGEACIVL SERCDGFLDCSDESDEKACSDELTVYKVQNLQWTADFSG
DVTLTWMRPKKMPASCVYNVYYRVVGESIWKTLETHSNKTNTVLKVLKPDTTYQVKV
QVQCLSKAHNTNDFVTLRTPEGLPDAPRNLQLSLPREAEGVIVGHWAPPIHTHGLIREYI
VEYSRSGSKMWASQRAASNTEIKNLLVNTLYTVRVAAVTSRGIGNWSDSKSITTIKGK

VIPPPDIHIDSYGENYLSFTLTMESDIKVNGYVVNLWAFDTHKQERRTLNFRGSILSHKV
 GNLTAHTSYEISAWAKTDLGDSPLAFEHVMTRGVPPAPSLKAKAINQTAVECTWTGP
 RNVVYGYIFYATSFLDLYRNPKSLLTSLHNKTVIVSKDEQYLFLVRVVVPYQGPSSDYVVV
 KMIPDSRLPPRHLHVVTGKTSSVIKWEPSYDSPDQDLYAIAVKDLIRKTDRSYKVCSR
 NSTVEYTLNKLEPGGKYHIIVQLGNMSKDSSIKITTVSLSAPDALKIITENDHVLLFWKSLA
 LKEKFNESRGYEIHMFDSAMNITAYLGNTTDNFFKISNLKMGHNYTFTVQARCLFGNQI
 CGEPAILLYDELGSGADASATQAARSTDVAAVVVPILFLILLSLGVGFAILYTKHRRRLQSS
 FTAFANSHYSSRLGSAIFSSGDDLGEDDEDAPMITGFSDDVPMVIA

SEQ ID No:172

GRWASGEMAPSGSLAVPLAVLVLLLWGAPWTHGRRSNVRVITDENWRELLEGDWMI
 EYAPWCPACQNLQPEWESFAEWGEDLEVNIAKVDVTEQPGLSGRFIITALPTIYHCKDG
 EFRRYQGPRTKKDFINFISDKEWKSIEPVSSWFGPGSVLMSSMSALFQLSMWIRTCHN
 YFIEDLGLPVWGSYTVFALATLFSGLLGLCMIFVADCLCPSKRRRPQPYPYPSKKLLSE
 SAQPLKKVEEEQEADEEDVSEEEAESKEGTNKDFPQNAIRQRSLGPSLATDKS

SEQ ID No:173

MVNYAWAGRSQRKLWWRSVAVLCKSVVRPGYRGGLQARRSTLLKTCARARATAPG
 AMKMVAPWTRFYNSCCLCCCHVRTGTILLGVWYLIINAVVLLILLSALADPDQYNFSSSE
 LGGDfefMDDANMCIAIAISLLMILICAMATYGAYKQRAAWIIPFFCYQIFDFALNMLV
 AITVLIYPNSIQEYIRQLPPNFPYRDDVMSVNPTCLVLIILLFISIILTFKGYLISC
 VWN CYRYINGRNSSDVLVYVTSNDTTVLLPPYDDATVNGAAKEPPPPYVSA

SEQ ID No:174

MEFYESAYFIVLIPSIVITVIFLFFWLFMKTLYDEVLAQKQREQKLIPTKTDKKAEKKKN
 KKKEIQNGNLHESDSESVPDFKLSDALAVEDDQVAPVPLNVETSSSVRERKKKEKK
 QKPVLEEQVIKESDASKIPGKKVEPVPTKQPTPPSEAAASKKPGQKKSNGSDDQD
 KKVELTMVPSKRQEALPLHQETKQESGSGKKASSKKQKTENVFVDEPLIHATTYIPLMD
 NADSSPVVDKREVIDLLKPDQVEGIQKSGTKKLKTETDKENAEVFKDFLLSLKTMMFS
 EDEALCVVDLLKEKSGVIQDALKKSSKGELTTLIHQLQEKDCKLLAAVKEDAAATKDRCKQ
 LTQEMMTEKERSNVVMTRMKDRIGTLEKEHNVFQNKIHSVYQETQQMQMKFQQVREQ
 MEAEIAHLKQENGILRDAVSNTTNQLESQSAELNKLQRQDYARLVNELTEKTGKLQQEE
 VQKKNAEQAAATQLKVQLQEAERRWEEVQSYIRKRTAEHEAAQQDLQSKFVAKENEVQ
 SLHSKLTDTLVSQQLEQRLMQLMESEQKRVNKEESLQMVGQDILEQNEALKAQIQQF

HSQIAAQTSASVLAELHKVIAEKDKQIKQTEDSLASERDRLTSKEEELKDIQNMNFLLKA
 EVQKLQALANEQAAAHELEKMQQS VYVKDDKIRLLEEQLQHEISNKMEEFKILNDQNKA
 ALKSEVQKLQTLVSEQPNKDVEQMEKCIQEKDEKLKTVEELLETGLIQUVATKEEELNAI
 RTENSSLTKEVQDLKAKQNDQVSFASLVEELKKVIHEKDGKIKSVEELLEAELLKVANKE
 KTVQDLKQEIKALKEEIGNVQLEKAQQLSITSKVQELQNLKGKEEQMNTMKAVLEEKE
 KDLANTGKWLQDLQEENESLKAHVQEVAQHNLKEASSASQFEELIEVLKEKGNELKRLE
 AMLKERESDLSSKTQLLQDVQDENKLFKSQIEQLKQQNYQQASSFPPHEELLKVISERE
 KEISGLWNELDSLKDAVEHQRKKNNDLREKNWEAMEALASTEKMLQDKVNKTSKERQ
 QQVEAVELEAKEVLKKLFPKVSVPSNLSYGEWLHGFEKKAKECMAGTSGSEEVKVLEH
 KLKEADEMHLLQLECEKYKSVLAETEGILQKLQRSVEQUEENWKVKVDESHKTIKQMQ
 SSFTSSEQELERLRSENKDIENLRREREHLEMELEKAEMERSTYVTEVRELKDLLTELQ
 KKLDSDSYSEAVRQNEELNLLKAQLNETLTKRTEQNERQKVAGDLHKAQQSLELIQSKI
 VKAAGDTTVIENSDVSPETESSEKETMSVSLNQTVTQLQQQLQAVNQQLTKEKEHYQVL
 E

SEQ ID No:175

MGALARALLPLLAQWLLRAAPELAPAPFTLPLRVAAATNRVVAPTPGPGPTPAERHADG
 LALALEPALASPAGAANFLAMVDNLQGDSGRGYYLEMLIGTPPQKLQILVDTGSSNFAV
 AGTPHSYIDTYFDTERSSTYRSKGFDVTVKYTQGSWTGFVGEDLVTPKGNTSFLVNIA
 TIFESENFFLPGIKWNGILGLAYATLAKPSSSLETFFDSLVTQANIPNVFSMQMCAGLP
 VAGSGTNGGSLVLGGIEPSLYKGDIWYTPIKEEWYYQIEILKLEIGGQSLNLDREYNAD
 KAIVDSGTTLLRLPQKVFDAVVEAVARASLIPEFSDGFWTGSQLACWTNSETPWSYFPK
 ISIYLRDENSSRSFRITILPQLYIQPMMGAGLNYE CYRFGISPSTNALVIGATVMEGFYVIF
 DRAQKRVGFAASPCAEIAGAAVSEISGPFSTEDVASNCVPAQSLSEPILWIVSYALMSVC
 GAILLVLIVLLLLPFRCQRRPRDPEVVNDESSLVRHRWK

SEQ ID No:176

QNQPYCRGLPDQDIISQLSQSPSQAAKSFYDRISFLIGSDSTHVIPGESPFNKSASVI
 RGQVLTADGTPLIGVNVSFFHYPEGYTITRQDGMDLVANGGASLTIVFERSPFLTQY
 HTVWIPWNVFYVMDTLVMKKEENDIPSCDLSGFVRPNPIVSSPLSTFFRSPEDSPIIPE
 TQLHEETTIPGTDLKSYLSSRAAGYKSVLKITMTQSIIPFNLMKVHLMVAVVGRLFQK
 WFPASNPLAYTFIWDKTDAYNQKVYGLSEAVVSVGYESCLDLTLWEKRTAILQGYEL
 DASNMGGWTLDKHHVLDVQNGILYKGNGENQFISQQPPVSSIMGNGRRRSISCPSN
 GQADGNKLLAPVALACGIDGSLYVGDFNYVRRIFPSGNVTSVLELRNKDFRHSSNPAHR

YYLATDPVTGDLVSDTNTRRIYRPKSLTGAKDLTKNAEVVAGTGEQCLPFDEARCGD
 GGKAVEATLMSPKGMAVDKNGLIYFVDGTMIRKVDQNGIISTLLGSNDLTSARPLTCCTS
 MHISQVRLEWPTDLAINPMDSIYVLDNNVVLQITENRQVRIAAGRPMHCQVPGVEYPV
 GKHAVQTTLLESATAIAVSYSGVLYITETDEKKINRIRQVTTDGEISLVAGIPSECDCKNDA
 NCDCYQSGDGYAKDAKLSAPSSLAASPDGTLIADLGNIRIRAVSKNKPPLLNSMNFYEV
 ASPTDQEYLIFDINGTHQYTDSLVTGDYLYNFSYSNDNDITAVTDNSGNTLIRRDPNRM
 PVRVVSPDNQVIWLTIGTNGCLKSMTAQGLELVLFTYHGNSGLLATKSDETGWTTFFDY
 DSEGRLTVTFPTGVVTNLHGDMDKAITVDIESSSREEDVSITSNLSSIDSFYTMVQDQL
 RNSYQIGYDGSLRIIYASGLDSHYQTEPHVLAGTANPTVAKRNMTLPGENGQNLVEWR
 FRKEQAQGKVNVFGRKLRVNGRNLLSVDFDRRTKTEKIYDDHRKFLLRIAYDTSGHPTL
 WLPSSKLMAVNVNTYSSTGQIASIQRGTTSEKVDYDGQGRIVSRVFADGKTWSYTYLEK
 SMVLLLHSQRQYIFEYDMWDRLSAITMPSVARHTMQTIRSIGYYRNIYNPPESNASIITDY
 NEEGLLLQTAFLGTSRRVLFKYRRQTRLSEILYDSTRVSFTYDETAGVLKTVNLQSDGFI
 CTIRYRQIGPLIDRQIFRFSEDGMVNARFDYSYDNSFRVTSMQGVINETPLPIDLYQFDDI
 SGKVEQFGKFGVIYYDINQIISTAVMTYTKHFDAHGRIKEIQYEIFRSLMYWITIQQYDNMG
 RVTKREIKIGPFANTTKYAYEYDVDGQLQTVYLNEKIMWRYNYDLNGNLHLLNPSNSAR
 LTPLRYDLRDRITRLGDVQYRLDEDGFLRQRGTEIFEYSSKGLLTRVYSGSGWTVIYR
 YDGLGRRVSSKTSLGQHLQFFYADLTYPTRITHVYNHSSSEITSLYYDLQGHLFAMEISS
 GDEFYIASDNTGTPLAVFSSNGLMLKQIQYTAYGEIYFDSNIDFQLVIGFHGGLYDPLTKL
 IHFGERDYDILAGRWTTPDIEIWKRIGKDPAPFNLYMFRNNNPASKIHDVKDYITDVNSW
 LVTFGFHLHNAIPGFPVPKFDLTEPSYELVKSQQWDDIPPIFGVQQQVARQAKAFLSLG
 KMAEVQVSRRRAGGAQSWLWFATVKSLIGKGVMLAVSQGRVQTNVLNIANEDCIKVA
 VLNNAFYLENLHFTIEKDTHYFIKTTTPESDLGTLRLTSGR

SEQ ID No:177

MPVTVTRTTITTTTSSSGLGSPMIVGSPRALTQPLGLLRLQLVSTCVAFSLVASVGAW
 TGSMGNWSMFTWCFCFSVTLLILIVECGLQARFPLSWRNFPITFACYAALFCLSASIYP
 TTYVQFLSHGRSRDHAIATFFSCIACVAYATEVAWTRARPGEITGYMATVPGLLKVLET
 FVACIIFAFISDPNLYQHQPALEWCVAVVAICFILAAIAILLNLGETNVLPPIPFPSFLSGLAL
 LSVLLYATALVLWPLYQFDEKYGGQPRRSRDVCSRSHAYYVCAWDRRLAVAILTAINL
 LAYVADLVHSAHLVFKV

SEQ ID No:178

PGGLLLGDVAPNFEANTTVGRIRFHDGLGDSWGLFSHPRDFTPVCTTELGRAAKLAPE
 FAKRNVKLIALSIDSVEDHLAWSKDINAYNCEEPTEKLPFFIIDDRNRELAILLGMLDPAEK
 DEKGMPVTARVVVFVFGPDKKLKLISILYPATTGRNFDEILRVVISLQLTAEKRVATPVDWK
 DGDSVMVLPTIPEEEEAKKLFPKGVFTKELPSGKKYLRYTPQP

SEQ ID No:179

MGTTASTAQQTVSAGTPFEGLQGSGTMDSRHSVIHSFQSTSLHNSKAKSIIIPNKVAPV
 VITYNCKEEFQIHDELLKAHYTLGRLSDNTPEHYLVQGRYFLVRDVTEKMDVLGTVGSC
 GAPNFRQVQGGLTVGGMGQPSLSGFRRVLQKLQKDGHRECVIFCVREEPVLFRADE
 DFVSYTPRDQNLHENLQGLPGPGRVESLELAIRKEIHDFAQSLSENTYHVYHNTEDLWG
 EPHAVAIHGEDDLHVTTEEVYKRPLFLQPTYRYHRLPLPEQGSPLEAQQLDAFVSVLRETP
 SLLQLRDAHGPPPALVFSCQMGVGRTNLGMVLGTLILLHRSGTTSQPEAAPTQAKPLP
 MEQFQVIQSFLRMVPQGRRMVEEVDRAITACAELHDLKEVVLENQKKLEGIRPESPAQ
 GSGSRHSVWQRALWSLERFYFLILFNYYLHEQYPLAFALSFSRWLCAHPELYRLPVTLS
 SAGPVAPRDLIARGSLREDDLVSPDALSTVREMDVANFRRVPRMPIYGTAQPSAKALG
 SILAYLTDAKRRLRKVVVWVSLREEAVLECDGHTYSLRWPGPPVAPDQLETLEAQLKAHL
 SEPPPGKEGPLTYRFQTCLTMQEVSQHRRACPGTYHRIPMPDFCAPREEDFDQLLE
 ALRAALSKDPGTGFVFSCLSGQQGRTTAMVVAVLAFWHIQGFPEVGEEELVSVPDAKF
 TKGEFQVVMKVQQLPDGHGVKEVDAALDTVSETMTPMHYHLREIIICTYRQAKAAKE
 AQEMRRLQLRSLQYLERVCLILFNAYLHLEKADSWQRPFSTWMQEVASKAGIYEILNE
 LGFPELESGEDQPFSRLRYRWQECSLEPSAPEDLL

SEQ ID No:180

MAQAKISAKAHEGRFCRSSSMADRSSLLES LDQLELRVEALRDAATAVEQEKEILLEMI
 HSIQNSQDMRQISDGEREELNLTANRLMGRTLTVEVSVETIRNPQQEESLKHATRIIDEV
 VSKFLDDLGNNAKSHLMSLYSACSSEVPPGPVDQKFQSIVIGCALEDQKKIKRRLETLLRN
 IDNSDKAIKLEHAKGAGSKSLQNTDGKFN

SEQ ID No:181

MRELEAKATKDVERNLSRDLVQEEEQLMEETEKEKDDKKKKEAAQKKATEQKIKVPEQI
 KPSVSQPQPANSNNGTSTATSTNNNAKRATANNQQPQQQQQQQQPQQQQPQQQPQ
 PQPQQQQPQQQPQALPRYPREVPPRFRHQEHKQLLKGQHFPVIAANLGSAVKVLNS
 QSESSALTNQQPQNNGEVQNSKNQSDINHSTSGSHYENSQRGPVSSTS DSSTNCKNA
 VVSDLSEKEAWPSAPGSDPELASECMDADSASSSESERNITIMASGNTGGEKDGLRNS

TGLGSQNKFVVGSSSNVHGGSSTGPWGFSHGAIISTCQSVDAPESKSESSNNRMN
 AWGTVSSSNGGLNPSTLNSASNHGAWPVLENNGLALKGPVGSGSSGINIQCSTIGQM
 PNNQSINSKVSGGUTHGTWGLQETCESEVSGTQKVSFGQPQNITTEMTPNNTN
 FMTSSLPNSGSVQNNELPSSNTGAWRVSTMNHPCMQAPSGMNGTSLSHLSNGESKS
 GGSYGTWGAYGSNYSGDKCSGPNGQANGDTVNATLMQPGVNGPMGTFQVNTNK
 GGGWESGAANSQSTSWSGSGNGANSGGSRRGWGTPAQNTGTNLPSVEWNKLPSN
 QHSNDSANGNGKTFTNGWKSTEEEDQGSATSQTNEQSSVWAKTGGTVESDGTEST
 GRLEEKGTGESQSRRRKIDQHTLLQSIVNRTDLDPRVLSNSGWGQTPIKQNTAWDTE
 TSPRGERKTDNGTEAWGSSATQTFNSGACIDKTSPNGNDTSSVSGWGDPKPALRWG
 DSKGSNCQGGWEDDSAATGMVKSQNQWGNCKEEKAAWNDSQKNKQGWGDGQKSS
 QGWSVSASDNWGETRNNHGEANKKSSSGSDRSVSGWNELGKTSSFTWGN
 NINPNNSSGWDESSKPTPSQGWGDPPKSNQLGWGDSSKPVSSPDWNKQQDIVGS
 WGIPPATGKPPGTGWLGPIPAPAKEEEPTGWEEPSPEISIRRMEIDDGTSAWGDPSK
 YNYKNVNWMWNKNVPNGNSRSDQQAQVHQLTPASAISNKEASSGSGWGEPWGEPOST
 PATTVDNGTSAWGKPIDSGPSWGEPIAAASSTSTWGSSVGPQALSKSGPKSMQDG
 WCGDDMPLPGNRPTGWEEEEDVEIGMWNSNSSQELNSSLNWPPYTKKMSSKGLSGK
 KRRRERGMMKGGNKQEEAWINPFVKQFSNISFSRDSPEENVQSNKMDLSGGMLQDK
 RMEIDKHSNLIGDYNRTVGKGPGSRPQISKESSMERNPYFDKDGIADESQNMQFMSS
 QSMKLPPNSALPNQALGSIAGLGMQNLNSVRQNGNPSMFGVGNTAAQPRGMQQPP
 AQPLSSSQPNLRAQVPPPLLSPQVPVSLKYAPNNGLNPLFGPQQVAMLNQLSQLNQ
 LSQISQLQRLLAQQQRAQSQRSPSGNRPQQDQQGRPLSVQQQMMQQSRQLDPNLL
 VKQQTPPSQQQPLHQPAKSFLDNVMPHTPELQKGSPINAFSNFPIGLNSNLNVNM
 DMNSIKEPQSRLRKWTWDSISVNTSLDQNSSKHGAISSGFRLEESPFWPYDFMNSSTS
 PASPPGSIGDGWPRAKSPNGSSVNWPPEFRPGEWKGYPNIDPETDPYVTPGSVIN
 NLSINTVREVDHLRDRNSGSSSLNTLPSTAWSSIRASNYNVPLSTAQSTSARNSD
 SKLTWSPGSVTNTSLAHELWKVPLPPKNITAPSRRPPPGLTGQKPPPLSTWDNSPLRIGG
 GWGNSDARYTPGSSWGESSSGRITNWVLKNLTPQIDGSTLRTLHMQHGPLITFHNL
 PHGNALVRYSSKEEVVKAQKSLHMCVLGNTTILAFASEEEISRFFAQSQLTPSPGWQ
 SLGSSQSRLGSLDCSHSFSSRTDLNHWNGAGLSGTNCGDLHGTSLWGTPHYSTSLW
 GPPSSSDPRGISSPSPINAFLSVDHLGGGGESM

SEQ ID No:182

MNHQQQQQQQKAGEQQLSEPEDMEMEAGDTDPPRITQNPVINGNVALSDGHNTAE
 EDMEDDTSWRSEATFQFTVERFSRLSESVPSCFVRNLPWKIMVMMPRFYPDRPHQK

SVGFFLQCNAESDSTSWSCHAQAVLKINYYRDEKSFSRRISHLFFKENDWGFSNFM
 AWSEVTDPKGFIKKVTFEVFVQADAPHGVAWDSKKHTGYVGLKNQGATCYMNSL
 LQLTFFTQNQLRAVYMMPTEGDDSSKSVPLALQRVFYELQHSDKPVGTTKLTKSFGWE
 TLDSFMQHDVQELCRVLLDNVENKMKGTCVEGTIPKLFRGKMSYIQCDEVYRSDRR
 EDYYDIQLSIKGKKNIFESFVDYVAVEQLDGDNKYDAGEHGLQEAEGVKFLTPVLHL
 QLMRFMYDPQTDQNIKINDRFEFPEQLPLDEFLKQTDPKDPANYILHAVLVHSGDNHGG
 HYVVYLNPKGDGKWCKFDDDVSRCTKEEAIENYGGHDDLSVRHCTNAYMLVYIRE
 SKLSEVLQAVTDHDIPQQLVERLQEEKRIEAQKRKERQEAHLYMQVQIVAEDQFCGHQ
 GNDMYDEEKVKYTVFKVLKNSSLAEFVQSLSQTMGFPQDQIRLWPMQARSNGTKRPA
 MLDNEADGNKTMIELSDNENPWTIFLETVDPELAASGATLPKFKDHDVMLFLKMYDPK
 TRSLNYCGHIYTPISCKIRDLLPVMCDRAGFIQDTSLILYEEVKPNLTERIQDYDVSLDKAL
 DELMDGDIIVFQKDDPENDNSELPTAKEYFRDLYHRVDVIFCDKTIPNDPGFVVTLSNRM
 NYFQVAKTVAQRLNTDPMLLQFFKSQGYRDGPGNPLRHNYEGTLRDLQFFKPRQPK
 KLYYQQLKMKITDFENRRSFKCIWLNSQFREEEITLYPDKHGCVRDLLEECKKABELGE
 KASGKLRLLEIVSYKIIGVHQEDELLECLSPATSRTFRIEEIPLDQVDIDKENEMLVTAHF
 HKEVFGTGFIPFLLRIHQGEHFREVMKRIQSLLDIQEKEFKFAIVMTGRHQYINEDEY
 EVNLKDFEPQPGNMSSHPRPWLGHDHFNKAPKRSRYTYLEKAIKIH

SEQ ID No:183

MATCAEILRSEFPEIDGQVFDYVTGVLHSGSADFESVDDLVEAVGELLQEVS GDSKDDA
 GIRAVCQRMYNTLRLAEPQSQGNSQVLLDAPQLSKITENYDCGTLPGLLKREQSSTV
 NAKKLEKAEARLAKQEKRSEKDTLKTSNPLVLEEASASQAGSRKESRLESSGKNKSY
 DVRIENFDVSFGDRVLLLAGADVNLAWGRRYGLVGRNGLGKTLKMLATRSLRVPAHIS
 LLHVEQEAGDDTPALQSVLESDSVREDLLRRERELTAQIAAGRAEGSEAAELAEIYAKL
 EEIEADKAPARASVILAGLGFTPQMQQQPTREFSGGWRMRRLALARALFARPDLDEP
 TNMLDVRAILWLENYLQTWPSTILVVSHDRNFLNIAITDIHLHSQRDGYRGDFETFIKS
 KQERLLNQQREYEAQQQYRQHQVFDIFRFRYNANRASQVQSKLKMELKPELKPVDE
 SEVVMKFPDGFEKFSPPIQLDEVDFYYDPKHVIFSRLSVSADLESRICVVGENGAGKST
 MLKLLLGD LAPVRGIRHAHRNLKIGYFSQHHVEQLDLNVSABELLARKFPGREEYRH
 QLGRYGISGELAMRPLASLSGGQKSRAFAQMTPCPNFYILDEPTNHLDMETIEALGR
 ALNNFRGGVILVSHDERFIRLVCRELWVCEGGGVTRVEGGFDQYRALLQEQRREGFL

SEQ ID No:184

MLFWHTQPEHYNQHNQSGSYLRDVLA^LPIFKQEEPQLSPENEARL^PPLQYVLCAATSPA
 VKLHEETLT^LNQGQSYEIRLLENRKL^GDFQDLNTKYVKSII^RVVFHD^RRLQYTEHQ^QLE
 GWRWSRP^GDRIL^DIPLS^VGILDPRASPTQLNAVEFLWDP^AKRASA^FI^QVHCISTEFTP
 RKHGGEKGVPFRVQIDTFKQNENGEYTEHLHSASCQIKVFKPKGADR^KQKT^DREKMEK
 RTAQEK^EKYQPSYETT^TILTECSPWPDVAYQVN^SAPSPSYNGSPNSFGLGEGNASPTHP
 VEALPVGSDHLLPSASIQDAQQWLHRNRF^SQFCRLFASFSGAD^LLKMSR^DDLVQICGP
 ADGIRLFNAIKGRNVRPKMTIYVCQELEQNRVPLQQKRDGS^GDSNL^SVYHAIFLEEL^TTL
 ELIEKIANLYSISPQHIHRVYRQGPTGIHVVSNEMVQNFQDESCFVLSTIKAESNDGYHII
 LKCGL

SEQ ID No:185

MASVT^LSEA^EKVYIVHGVQEDLRVDGRGCEDYRCVEVETDVSNTSGSARV^KL^GH^TDI
 LVGVKAEMGTPKLEKPNEGYLEFFVDCSASATPEFEGRG^GDDLGTEIANTLYRIFNNKS
 SVDLK^TLCISPREHCWVLYVDVLL^LECGGNLFDAISIAVKAALFNTRIPRV^RVLEDEEGSK
 DIELSDDPYDCIRLSVENVPCIVTLCKIGYRHVV^DATLQEEACSLASLLVS^VTSKG^VTCM
 RKVGKGSLDPESIFEMMETGKRVGKVLHASLQS^VLKEESLGPKRQKVGF^LG

SEQ ID No:186

MAWVLKMDEVIESGLVHDFDASLSGIGQELGAGAYSMSDV^LALPIFKQEDSSLPLDGET
 EHPPFQYVMCAATSPAVKLHDET^LTYLNQGQSYEIRMLDNRK^MGD^MPEINGKL^VKSIIR
 VVFHD^RRLQYTEHQ^QLEGWKWN^RPGDR^LLD^LIPMSVGIIDTRTNPSQLNAVEFLWDP
 AKRTSA^FI^QVHCISTEFTPRKHGGEKGVPFR^IQVDTFKQNENGEYTD^HLHSASCQIKVFK
 PKGADR^KQKT^DREKMEKRTAHEKEKYQPSYDTT^ILMRLEPIIEDAVEHEQKKSSKRT
 LPADYGDSLAKRGSCSPWP^DAPTAYVNNSPSPAPTFTSPQQSTCSV^PDSN^SSPNHQ
 GDGASQTSGEQIQPSATIQETQQWLLKNRFSSYTRLFSN^FSGAD^LL^KLTKEDLVQICGA
 ADGIRLYNSLKSRSVRPRLTIYVCREQPSSTVLQGQQQAASSASENGSGAPYVYHAIYL
 EEMIASEVAR^KLALVFNIPLHQINQVYRQGPTGIHILVSDQM^VQNFQDESCFLF^STVKAE
 SSDGI^HILK

SEQ ID No:187

MAWALKLPLADEVIESGLVQDFDASLSGIGQELGAGAYSMSDV^LALPIFKQEESSLPPD
 NENKILPFQYVLCAATSPAVKLHDET^LTYLNQGQSYEIRMLDNRK^LGELPEINGKL^VKSIF
 RVVFHD^RRLQYTEHQ^QLEGWRWN^RPGDR^ILD^IIPMSVGIIDPRANPTQLNTVEFLWDP
 AKRTSVFIQVHCISTEFTMRKHGGEKGVPFRVQIDTFKENENGEYTEHLHSASCQIKVFK

PKGADRQKQTDREKMEKRTPHEKEKYQPSYETTILTECSPWPEITYVNNSPSPGFNSS
 HSSFSLGEGNNGSPNHQPEPPPPPVTDNLLPTTPQEQQWLHRNRNSTFTRLFTNFSGA
 DLLKLTRDDVIQICGPADGIRLFNALKGGRMVRPRLTIVCQESLQLREQQQQQQQQK
 HEDGDSNGTFFVYHAIYLEELTAVELTEKIAQLFSISPCQISQIYKQGPTGIHVLISDEMIQ
 NFQEEACFILDTMKQETNDSYHIILK

SEQ ID No:188

MSTPPLAASGMAPGPFAGPQAQQAAREVNTASLCRIGQETVQDIVYRTMEIFQLLRNM
 QLPNGVTYHTGTYQDRLTLQDNLRQLSVLFRKRLVYDKCNENCGMDPIPVEQLIPY
 VEEDGSKNDDRAGPPRFASEERREIAEVNKKLKQKNQQLKQIMDQLRNLIWDINAMLA
 MRN

SEQ ID No:189

MAQKMDCGAGLLGFQAEASVEDSALLMQTLMEAIQISEAPPTNQATAAASPQSSQPPT
 ANEMADIQVSAAAARPNSAFKVQNATTKGPNVYDFSQAHNAKDVPNTQPKAAFKSQ
 NATSKGPNAAYDFSQAATTGELAANKSEMAFKAQNATTKVGPNATYNFSQLNANDLA
 NSRPKTPFKAWNDTTKAPTADTQTQNQNVNQAKMATSQADIETDPGISEPDGATAQTSAD
 GSQAQNLESRTIIRGKRTRKINNLNVEENSSGDQRRAPLAAGTWRSAPVPVTTQNPPG
 APPNVLWQTPLAWQNPSGWQNQTARQTTPPARQSPPARQTPPAWQNPAWQNPAWQNPAW
 PNPVIWQNPVIWPNIWPNPIWWPGPVVWPPLAWQNPPGWQTTPGWQGPPDWQ
 GPPDWPLPPDWPLPPDWPLPTDWPLPPDWIPADWIPPPDWQNLRPSPNLRPSPNSRA
 SQNPGAAQPRDVALLQERANKLVKYLMLKDYTKVPIKRSEMLRDIIREYTDVYPEIIERA
 CFVLEKKFGIQLKEIDKEEHLYIISTPESLAGILGTTKDTPKLGLLLVLGVIFMNGNRASE
 AVLWEALRKMGRLPGVRHPLLGDLRKLLTYEFVKQKYLDYRRVPNSNPPEYEFLWGLR
 SYHETSKMKVLRFIAEVQKRDPRDWTAQFMEAADEALDALDAAAAEAEARAEARTRM
 GIGDEAVSGPWSWDDIEFELLTWDEEGDFGDPWSRIPFTFWARYHQNARSRFPQTFA
 GPIIGPGGTASANFAANFGAIGFFWVE

SEQ ID No:190

RRRLDADPAAGRRAAPAPKRLSVPDAPRPTPTMKRASAGGSRLLAWVLWLQAWQVAA
 PCPGACVCYNEPKVTTSCPQQGLQAVPGVIPAASQRIFLHGNRISHVPAASFRACRNLT
 ILWLHSNVLARIDAAFTGLALLEQLDLSDNAQLRSVDPATFHGLGRLHTLHLDRCGLQE
 LGPGLFRGLAALQYLYLQDNALQALPDDTFRDLGNLTHLFLHGNRISSVPERAFRGLHS
 LDRLLLHQNRVAHVPHAFRDLGRLMTLYLFANNLSALPTEALAPLRALQYLRNDNPW

VCDCRARPLWAWLQKFRGSSSEVPCSLPQRLAGRDLKRLAANDLQGCAVATGPYHPI
 WTGRATDEEPLGLPKCCQPDAADKASVLEPGRPASAGNALKGRVPPGDSPPNGSG
 PRHINDSPFGTLPGSAEPPLTAVRPEGSEPPGFPTSGPRRRGCSRKNRTRSHCRLGQ
 AGSGGGGTGDSEGSGALPSLTCSLPLGLALVLWTVLGPC

SEQ ID No:191

MAEQEPTAEQLAQIAAENEEDEHNVYKPPAQKSIQEIQELDKDDESLRKYKEALLGRV
 AVSADPNVPNVVVTGLTVCSSAPGPLEDLTDLESFKKQSFVLKEGVEYRIKISFRVN
 REIVSGMKYIQQHTYRKGVKIDKTDYMGSYGPRAEEYEFLTPVEEAPKGMLARGSYSIK
 SRFTDDDKDTHLSWEWNLTIKKDWDKD

SEQ ID No:192

MAKHEQILVLDPPDLKFKGPFDTVVTTNLKLRNPSDRKVCVKTTAPRRYCVRPNSG
 IIDPGSTVSVMLQPFDYDPNEKSCHKFMVQTIFAPPNTSDMEA VWEAKPDELMDSK
 LRCVFEMPNENDKLNDMEPSKAVPLNASQDGPMKPHSVSLNDTETRKLMEECRKL
 QGEMMKLSEENRHLRDEGLRLRKVAHSDKPGSTSTASFRDNVTSPPLPSLLVIAIFIGF
 FLGKFIL

SEQ ID No:193

MGAGATGRAMDGPRLLLLLGVSLGGAKEACPTGLYTHSGECKACNLGEGVAQPC
 GANQTVCEPCLDSVTFSVDVSATEPCKPCTECVGLQSMSAPCVEADDAVCRCAYGY
 QDETTGRCEACRVCEAGSGLVFSCQDKQNTVCEECPDGTYSDDEANHVDPCLPCTVCE
 DTERQLRECTRWRADAEEIPGRWITRSTPPEGSDSTAPSTQEPEAPPEQDLIASTVAG
 VVTTVMGSSQPVTRGTTDNLIPVYCSILA VVVGLVAYIAFKRWNSCKQNKGANSRP
 VNQTPPPGEKEKLHSDSGISVDSQSLHDQQPHTQTASGQALKGDGGLYSSLPPAKREEV
 EKLLNGSAGDTWRHLAGELGYQPEHIDSFTHEACPVRALLASWATQDSATLDALLAAL
 RRIQRADLVESLCSESTATSPV

SEQ ID No:194

MAQRKNAKSSGNSSSSGSGSGSTSAGSSSPGARRET KHGGHKNGRKGGSGTSFFT
 WFMVIALLGWVWTSAVWWFDLVDYEEVLGKLGIYDADGDGDFDVDDAKVLLGLKERST
 SEPAVPPEEAEPHTEPEEQVPVEAEPQNIEDEAKEQIQSLLHEMVHAEHVEGEDLQQE
 DGPTGEPQQQEDDEFLMATDVDDRFTETLEPEVSHHEETEHSYHVEETVSQDCNQDMEM
 MSEQENPDSSEPVVEDERLHHDTDDVTYQVYEEQAVYELENEGIEITEVTAPPEDNPV

EDSQVIVEEVSIFFVEEQQEVPETNRKTDDPEQKAKVKKKKPKLLNKFDKTIKAELDAA
 EKLRKRGKIEEAVNAFKELVRKYPQSPRARYGKAQCEDDLAEKRRSNEVLRGAIETYQE
 VASLPDVPADELLKLSLKRRSDRQQFLGHMRGSLTLQRLVQLFPNDTSKNDLGVGYLL
 IGDNDNAKKVYEEVLSVTPNDGFAKVHYGFILKAQNKIAESIPYLKEGIESGDPGTDDGR
 FYFHLG DAMQR VGNKE AYKW YELGH KRG HFAS V W QR SLIN V NGL KA Q PC GP KET GYT
 QLVKS LERNW KLIR DEGLA VMDKA KGL F LPEDENL REKG DWSQFTL W QQG RR NEN AC
 KGAPKT CTLLEKF PETTGC RRGQIKY SIMHPG THV WPHT GPTN CRLRMH GLV IP KEGC
 KIRC ANETKTWE EGKV LIF DDSFE HEVW QDASSF RLIFIV DVWH PELTPQQRRSLPAI

SEQ ID No:195

KMATPLAVNSAASLWGPYKDIWHKVGNALWRRQPEAVHLLDKILKKHKPDFISLFKNPP
 KNVQQHEKVQKASTEGVAIQGQQGTRLLPEQLIKEAFILSDLFDIGELAAVELLAGEHQ
 QPHFPLTRGLVAVLLYWDGKRCIANSLKALIQSRRGKTWTLELSPELASMTTRFTDEL
 MEQGLTYKVLTVSQIDVNNEFEKLQRERGLGSEKHRKEVSDLIKECRQSLAESLFAWA
 CQSPLGKEDTLLIGHLERVTVEANGSLDAVNALLMALLYCFDISFIEQSTEERDDMIHQ
 LPLLTEKQYIATIHSRLQDSQLWKLPGHQATVRLAWALALRGISQLPDVTALAEFTEADE
 AMAELAIADNVFLFLMESVVVSEYFYQEEFYIRR VHNLTDFALMPMKVKQLRNRADED
 ARMIHMSMQMGNEPPISLRRDLEHLMILLIGELYKKNPFHLELALEYWCPTEPLQTPTIM
 GSYLGVAHQRPPQRQVVL SKFVRQM DLLPPTIYIPYLKMLQGLANGPQCAHYCFSLL
 KVNGSSHVENIQGAGGSPVSWEHFFHSLMLYHEHLRKDLPSADSVQYRHLSRGITQK
 EQDGLIAFLQLTSTIITWSENARLACCEHPQWTPVVVILGLLQCSIPPVLKAELLKTLAAGF
 KSPEIAASLWQSLEYTQILQTVRIPSQRQAIGIEVELNEIESRCEEYPLTRAFCQLISTLVE
 SSFPSNLGAGLRPPGFDPYLQFLRDSVFLRFRTRAYRRAEKWEVAEVLEVFYKLLR
 DYEPQLED FVDQFVELQGEEIIAYKPPGFSLMYHLLNESPMLELALSLEEGVKQLDTYA
 PFPGKKHLEKAVQHCLALLNLTQKENLFMDLLRESQLALIVCPLEQLLQGINPRTKKAD
 NVVNIARYLYHGNTNPELAFESAKILCCIS CNSNIQIKLVGDFTHDQSISQKLMAGFVECL
 DCEDAEEFVRLEEGSELEKKLVAIRHETRIHILNLLITSLECNPPNLALYLLGFELKKPVST
 TNLQDPGVLCPR TCLHAILNILEKGTEGRTGPVAVRESPQLAELCYQVIYQLCACSDTS
 GPTMRYLRTSQDFLFSQLQYLPFSNKEYEISMLNQMSWLMKTASIELRVTSNRQRSHT
 QRLLHLLLDDMPVKPYSDGEGGIEDENRSVSGFLHFDTATKVRKILNILD SIDS QEIPE
 PLQLDFFDRAQIEQVIANCEHKNLRGQTCNVKLLHRLVVAEVNALQGMAAIGQRPLLM
 EEISTVLQYVVGRNKLLQCLHAKRHALESWRQLVEIILTACPQD LIQAEDRQLIIRDILQDV
 HDKILDDEAQELMPVVAGAVFTLTAHLSQAVL TEQKQTSVL GPAEAHYAFMLDSCFTS
 PPPEENPLVGFASIGDSSLYIILKKLLDFILKTGGGFQRVRTHLYGSLLYYLQIAQR PDEP

DTLEAAKKTWERTAPEDVFSKLQRENIAIIIESYGAALMEVVCRDACDGHEIGRMLA
 ALLDRIVSVDKQQQWLLYLSNSGYLKVLVDSLVEDDRTLQSLLTPQPPLLKALYTYESK
 MAFLTRVAKIQQGAELLRSGVIVRLAQCQVYDMRPETDPQSMFGMRDPPMFIPTPVD
 RYRQILLPALQLCQVILTSSMAQHLQAAGQVLQFLISHSDTIQAILRCQDVSA
 GSLQELAL
 LTGIISKAALPGILSELDVDVNEGSLMELQGHIGRFQRQCLGLLSRGGS
 DRQFKFQD
 DNVEGDKVSKKDEIELAMQQICANVMEYCQSLMLQSSPTFQHAVCLFTPSLSETVNRD
 GPRQDTQAPVVPYWRLPGLGIIYLLQSA
 NFFSYYDSHRQSVSKLQNVEQLPPDEIK
 ELCQSVMPAGVDKISTAQKV
 LARRRLVKVINNRAKLLS
 LCSFIETCLFILWRHLEY
 YLL
 HCMPTDSQDSLFA
 SRTLFKSRRLQDSFA
 SETNLD
 FRSGLAIVSQHDLDQLQADAINAFG
 ESLQKKLLDIEGLYSKVR
 SRYSFIQALVRRIRGLL
 RISRN

SEQ ID No:196

MSFLKSFP
 PPPGPAEGLLRQQPDTEAVLN
 GKGLGTGTL
 YIAESRLSWLDGSGLGFSLEY
 PTISLHALSRDRSDCLGEHLYVMVNAK
 FEEESKEPV
 VADEEEEDS
 SDDVE
 PITEFRFVPS
 DKS
 ALEAMFTAMCEC
 QALHPDPE
 EDSDDYD
 GEYD
 VEA
 HEQGQGD
 IPTFY
 T
 YE
 EGL
 SHLTAEGQATLERLEG
 MLSQS
 VSSQYN
 MAG
 VR
 TEDS
 IRDY
 EDG
 MEV
 DTT
 PT
 VAGQFE
 DADVDH

SEQ ID No:197

HNAASPGGARGHRVPLTEACKDSRIGGMMKTLLL
 FVG
 LLL
 WESGQV
 LGDQTV
 SDNEL
 QEMSNQGS
 KYVN
 KEIQNA
 VNGVK
 QIKT
 LIEKT
 NEER
 K
 TLL
 S
 N
 L
 E
 EAKKK
 KEDAL
 NETRE
 SETKL
 KELPGVC
 NETMMAL
 WEECK
 PCLK
 QT
 CMKF
 YARV
 CRSG
 SGL
 VGR
 QLE
 EFLNQS
 SPFYFW
 MN
 GDR
 IDSL
 LLE
 NDR
 RQQ
 THML
 DV
 M
 QDH
 FSR
 RASS
 II
 I
 DELF
 QDR
 FFT
 REP
 QD
 TYH
 YLPFSL
 PHRR
 PFFF
 PKS
 RIV
 RSL
 MPF
 SPY
 EPL
 NF
 HAM
 FQP
 FLEM
 I
 HEAQ
 QQAM
 DIHFHS
 PAFQH
 PPTE
 FIRE
 GDD
 DRT
 VC
 RE
 IRHN
 STG
 CLR
 MKD
 QC
 DK
 CRE
 IL
 SV
 DC
 CST
 NN
 PSQAK
 LR
 REL
 DESL
 QVA
 ERL
 TRK
 YN
 ELL
 KSY
 QW
 KML
 NT
 SS
 L
 EQL
 NEQ
 FN
 W
 S
 R
 LAN
 LT
 QGED
 QYYLR
 VTT
 VASHT
 SDV
 PSGV
 TE
 VVV
 KLF
 DSD
 P
 IT
 TVP
 VE
 VSR
 KNPK
 FMET
 VAE
 KAL
 QEYRK
 KHREE

SEQ ID No:198

EKSGGP
 GTRER
 EKRE
 ERQSA
 WGR
 KER
 GREG
 W
 VRR
 RSA
 AN
 PRR
 RAW
 SPSQNS
 SPS
 RS
 RSQ
 GGG
 CDR
 QPC
 MMH
 RLFC
 ILL
 AA
 VSG
 AE
 GW
 YY
 GC
 DE
 ELV
 G
 PLY
 AR
 SLG
 ASS
 YY
 SLL
 TAP
 PRF
 FAR
 LH
 GIS
 GW
 SPR
 IGD
 DP
 NP
 PW
 L
 QID
 LM
 KK
 HR
 I
 RAV
 AT
 Q
 GS
 FN
 SW
 DW
 V
 TRY
 MLL
 YG
 DR
 VD
 SW
 TPFY
 QR
 GH
 N
 ST
 FF
 GN
 V
 NE
 AV
 VR
 HDL
 HF
 HT
 AR
 Y
 I
 RIV
 PL
 WNP

RGKIGLRLGLYGCPTYKADILYFDGDDAISYRFPRGVSRSLWDVFAFSKTEEKDGLLLHA
 EGAQGDYVTLEGAHLLLHMSLGSSPIQPRPGHTVSAGGVNDQHWHYVRVDRFG
 RDVNFTLDGYVQRFILNGDFERLNLDTEMFIGGLVGAARKNAYRHNFRCIENVIFNRV
 NIADLAVRRHSRITFEGKVAFRCLDPVPHPINFGGPHNFVQVPGFPRRGRLAVSFRFRT
 WDLTGLLFSRLGDGLGHVELTSEGQNVNSIAQSGRKKLQFAAGYRLNDGFWHEVNF
 VAQENHAVISIDDVEGAEVRSYPLIIRTGTSYFFGGCPKPASRWDCHSNQTAFHGCM
 ELLKVDGQLVNLTLVEGRRLGFYAEVLFDTCGITDRCSPNMCEHDGRCYQSWDDFICY
 CELTGYKGETCHTPLYKESCEAYRLSGKTSGNFTIDPDGSGPLKPFVVYCDIRENRAWT
 VVRHDRLWTRVTGSSMERPFLGAIQYWNASWEEVASALANASQHCEQWIEFSCYNR
 LLNTAGGYPYSFWIGRNNEEQHFYWGGSQPGIQRCACGLDRSCVDPALYCNCADQPQ
 WRTDKGLTFVDHLPVTQVVGDTNRSTSEAQFFLRPLRCYGRNNSWNTISFHTGAALR
 FPPIRANHSLDVSFYFRTSAPSGVFLENMGGPYCQWRPPYVRVELNTSRDVVFADFVG
 NGDENLTVHSDDFEFNDEWHLVRAEINVKQARLRVDHRPWVLRPMPLQTYIWMEYD
 QPLYVGSAELKRRPFVGCLRAMRLNGVTLNLEGRANASEGTSPNCTGHCAHPRLPCF
 HGGRCVERYSYYTCDCDLTAFDGPYCNHDIGGFFEPGTWMRYNLQSArsaAREFSH
 MLSRPVPGYEPGYIPGYDTPGYVPGYHGPGRYRLPDYPRPGRPVPGYRGPVNVNTGEE
 VSFSFSTSSAPAVLLYVSSFVRDYMMAVLIKDDGTLQLRYQLGTSPYVYQLTTRPVTDGQ
 PHSINITRVYRNLFIQVDYFPLTEQKFSLLVDSQLDSPKALYLGRVMETGVIDPEIQRYNT
 PGFSGCLSGVRFNNVAPLKTHFRTPRPMTAELAEALRVQGELSESNCGAMPRLVSEVP
 PELDPWYLPPDFPYYHDEGWVAILLGFLVAFLLLGLVGMVLFYLQNHYKGSYHTNEP
 KAAHEYHPGSKPPLPTSGPAQVPTPTAAPNQAPASAPAPAPTPAPAPGPRDQNLPQIL
 EESRSE

SEQ ID No:199

MASRLLRGAGTLAAQALRARGPSGAAAMRSMASGGGVPTDEEQATGLEREIMLAKK
 GLDPYNVLAPKGASGTREDPNLVPSISNKRIVGCICEEDNTSVWWFWLHKGEAQRCPR
 CGAHYKLVPQQLAH

SEQ ID No:200

MAEDMETKIKNYKTAPFDSRFPQNQNQTRNCWQNYLDFHRCQKAMTAKGGDISVCEWY
 QRVYQSLCPTSWVTDWDEQRAEGTFPGKI

SEQ ID No:201

MAPEVLPKPRMRGLLARRLRNMAVAFVLSLGVAALYKFRVADQRKKAYADFYRNYDV
MKDFFEMRKAGIFQSVK

SEQ ID No:202

MAGLQLMTPASSPMGPFFGLPWQQEAIHDNIYTPRKYQVELLEAALDHNTIVCLNTGSG
KTFIAVLLTKELSYQIRGDFSRNGKRTVFLVNSANQVAQQSAVRTHSDLKVGESNLE
VNASWTKERWNQEFTKHQVLIMTCYVALNVLKNGYLSLDINLLVDECHLAILDHPYR
EIMKLCENCPSCPRLGLTASILNGKCDPEELEEKIQKLEKILKSNAETATDLVVLDRTS
QPCEIVVDCGPFTDRSGLYERLLMELEEAALNFINDCNISVHSKERDSTLISKQILSDCRAV
LVVLGPWCADKVAGMMVRELQKYIKHEQEELHRKFLLFTDFLRKIHALCEEHFSPASL
DLKFVTPKVIKLLIEILRKYKPYERQQFESVEWYNRNRNQDNYSWSDSEDDDEEIEEK
EKPETNFPSPFTNILCGIIFVERRYTAVVNLRLIKEAGKQDPDELAYISSNFTGHGIGKNQP
RNKQMEAEFRKQEEVLRKFRAHETNLLIATSIVEEGVDIPKCNLVRFDLPTEYRSYVQS
KGRARAPISNYIMLADTDKIKSFEEDLKYKAIEKILRNKCSKSVDTGETDIDPVMDDDDV
FPPYVLRPDDGGPRVTINTAIGHINRYCARLPSDPFTHLAPKCRTRLELPDGTYSTLYLPI
NSPLRASIVGPPMSCVRLAERVVALICCEKLHKIGELDDHLMMPVGKETVKYEEELDHDE
EETSVPGPGSTKRRQCYPKAYPECLRDSYPRPDQPCYLYVIGMVLTTPLPDELFRRR
KLYPPEDTTRCFGILTAKPIPQIPHFPVYTRSGETISIELKKSGFMLSQMLELITRLHQYI
FSHILRLEKPALEFKPTDADSAYCVLPLNVVNDSSTLIDFKFMEDIEKSEARIGIPSTKYT
KETPFVFKLEDYQDAVIIPRYRNFDQPHRFYVADVYDLTPLSKFPSPEYETFAEYYKT
YNLDLTNLNQPLLDVDHTSSRLNLLTPRHLNQKGKALPLSSAEKRKAKWESLQNQKILV
PELCAIHIPASLWRKAVCLPSILYRLHCLLTAELRAQTASDAGVGVRSLPADFRYPNL
DFGWKKSIDSKSFISISNSSAENDNYCKHSTIVPENAAHQGANRTSSLENHDQMSVNC
RTLLSESPGKLHVEVSADLTAINGLSYNQNLANGSYDLANRDFCQGNQLNYYKQEIPVQ
PTTSYSIQNLYSYENQPQPSDECTLLSNKYLDGNANKSTSDGSPVMAVMPGTTDTIQLV
KGRMDSEQSPSIGYSSRTLGPNGLQLQALTNSADGFNLERLEMLGDSFLKHAITTYL
FCTYPDAHEGRLSYMRSKKVSNCNLYRLGKKGLPSRMVVSIFDPPVNWLPPGYVNN
QDKSNTDKWEKDEMTCDCMLANGKLDDEDYEEEDEEEESLMWRAPKEEADYEDDFLE
YDQEHIRFIDNMLMGSGAFVKKISLSPFSTTDSAYEWKMPKKSSLGSMPFSSDFEDFDY
SSWDAMCYLDPSKAVEEEDDFVVGFWNPSEENCVGVTGKQSISYDLHTEQCIADKSIAD
CVEALLGCYLTCGERAAQLFLCSLGLKVLPIKRTDREKALCPTRENFSQQKNLNSVS
CAAASVASSRSSVLKDSEYGCLKIPPRCMFDHPDADKTLNHLISGFENFEKKINYRFKNK
AYLLQAFTHASYHYNTITDCYQRLEFLGDAILDYLIKHYEDPRQHSPGVLTDLRSALVN
NTIFASLAVKYDYHKYFKAVSPELFHVIDDFVQFQLEKNEMQGMDSELRRSEEDEEKEE

DIEVPKAMGDIFESLAGAIYMDSGMSLETWQVYYPMRPLIEKFSANVPRSPVRELLE
 MEPEAKFSPAERTYDGKVRVTVEVVGKGKFKGVGRSYRIAKSAAARRALRSLKANQP
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SEQ ID No:203

MRLLAGWLCLSLASVWLARRMWTLRSPLTRSLYVNMTSGPGGAAAAGGRKENHQW
 YVCNREKLCESLQAVFVQSYLDQGTQIFLNNIEKSGWLFIQLYHSFVSSVFLFMSRTS
 INGLLGRGSMVFSPDQFQRLLKINPDWKTHRLLLGAGDGEVTKIMSPHFEEIYATELS
 ETMIWQLQKKYRVLGINEWQNTGFQYDVISCLNLLRCDQPLTLLKDIRSVLEPTRGR
 VIALVLPFHPYVENVGGKWEKPSEILEIKGQNWEEQVNSLPEVFRKAGFVIEAFTRLPY
 LCEGDMYNDYYVLDDAVFVLKPV

SEQ ID No:204

PPRASFAAAVAAAARDSSRAVMADPAAPTPAAPAPAPAQAQAPAPAPEAVPAPAAAPVPAPA
 PASDSASGPSSDFGPEAGSQRLLFSHDLVSGRYRGSVHGLVRLIHGEDSDSEGESEE
 RGSSGCSEAGGAGHEEGRASPLRRGYVRVQWYPEGVKQHVETKLKLEDRSVVPRD
 VVRHMRSTDQCCTVIDVNIDCAVKLIGTNCIYPVNSKDLQHIWPFMYGDYIAYDCWL
 KVDLKNQIILKLSNGARCSMNTEDGAALKYDVCPHVSDSGLFFDDSYGFYPGQVLIGPA
 KIFSSVQWLSGVKPVLSKFRVVVEEVQVELKVTWITKSFCPGGTDVSPPPSVIT
 QENLGRVKRLGCFDHAQRQLGERCLYVFPAKVEPAKIAWECPEKNCAQGEGSMAKKV
 KRLLKKQVVRIMSCSPDTQCSRHSMEDPDKKGESKTSEAESASPEETPDGSASPVE
 MQDEGAEEPHEAGEQLPPFLLKEGRDDRLHSAEQDADDEAADDTDDTSSVTSSASST
 TSSQSGSGTSRKSIPLSIKLNKRKHKRKKNKITRDFKPGDRVAVEVTTMTSADVMWQ
 DGSVECNRNSNDLFPVHHLDNNEFCPGDFVVDKRVQSCPDPAVYGVVQSGDHIGRTC
 MVKWFKLPSGDDVELIGEEEDVSVYDIADHPDFRRTTDIVIRIGNTEDGAPHKEDEPS
 VGQVARVDVSSKVEVVWADNSKTIILPQHLYNIESEIEESDYDSVEGSTSGASSDEWED
 DSDSWETDNGLVEDEHPKIEEPPIPLEQPVAPEDKGVVISEEAATAAVQGAVAMAAMP
 AGLMEKAGKDGPBKSFRELKEAIKILESLKNMTVEQLLTGSPTSPTEPEKPTREKKFLD
 DIKKLQENLKKLDNVAIVEEEKMEAVERKEDKPEGQSPVKAEPSETPVLCQQC
 GGKPGVTFTSAKGEVFSVLEFAPSNSFKKIEFQPPEAKKFFSTVRKEMALLATSLPEGI
 MVKTFEDRMDLFSALIKGPTRTPYEDGLYLFIDQLPNIYPAVPPHFCYLSQCSGRLNPNL
 YDNGKVCVSLLGWTIGKTERWTSKSSLQVLISIQGLILVNEPYYNEAGFDSDRGLQE
 GYENSRCYNEMALIRVVQSMTQLVRRPPEVFEQEIRQHFSTGGWRLVNRIESWLETHA
 LLEKAQALPNGVPKASSSPEPPAVAELSDGQQEPEDGGPAPGEASQGSDSEGGAQS

LASASRDHTDQTSETAPDASVPPSVPKKRRKSYRSFLPEKSGYPDIGFPLFPLSKGFIK
SIRGVLTQFRAALLEAGMPECTEDK

SEQ ID No:205

MPGSAAKGSELSERIESFVETLKRGGGPRSSEEMARETLGLLRQIITDHRWSNAGELM
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LNEDFSFHQAQLQSNIIEAINELLVELEGTMENIAAQALEHIHSNEVIMTIGFSRTVEAFLK
EAARKRKFHVIVAECAFPCQGHHEMAVNLSKAGIETTVMTDAIFAVMSRVNKVIIGTKTIL
ANGALRAVTGTHTLALAAKHHSTPLIVCAPMFKLSPQFPNEEDSFHKFVAPEEVLPFTE
GDILEKVSVHCPVFDYVPPELITLFISNIGGNAPSXIYRLMSELYHPDDHVL

SEQ ID No:206

MRCCHICKLPGRVMGIRVLRLSLVVILVLLLVAGALTALLPSVKEDKMLMLRREIKSQGK
STMDSFTLIMQTYNRTDLLLKLLNHQAVPNLHKVIVVWNNGEKAPDELWNSLGPHPPIP
VIFKQQTANRMNRNLQVFPELETNAVLVDDDTLISTPDLVAFSVWQQFPDQIVGFVP
RKHVSTSSGIYSYGSFEMQAPGSGNGDQYSMVNLIGASFFNSKYLELFQRQPAAVHALID
DTQNCDIAMNFIIAKHIGKTSGIFVKPVNMDNLEKETNSGYSGMWHRAEHALQRSYCI
NKLVNIYDSMPLRYSNIMISQFGFPYANYKRKI

SEQ ID No:207

MAAVAAVAARRRSWASLVLAFGLVCLGITLAVDRSNFKTCEESSFCKRQRSIRPGLSP
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VADPPIARLSVSGRDENSVELTMAEGPYKIILTARPFRLDLLEDRSLLSVNARGLLEFEH
QRAPRVSFSDKVNLTGSIWDKIKNLFSRQGSKDPAGEGDGAQPEETPRDGDKPEETQG
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GEPYRLYNLDVFQYELYNPMALYGSVPVLLAHNPHRDLGIFWLNAETWVDISSNTAGK
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FSLGYHQSRWNYRDEADVLEVDQGFDDHNLPCDVIWLDIEHADGKRYFTWDPSRFPQ
PRTMLERLASKRRKLVAIVDPHIKVDSGYRVHEELRNGLYVKTRDGSDYEGWCWPGS
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AHLDTGRRREPWLPSQHNDIIRDALGQRYSLLPFWYTLLYQAHREGIPVMRPLWVQYP
QDVTTFNIDDQYLLGDALLVHPVSDSGAHGVQVYLPQQGEVWYDIQSYQKHHGPQTLY

LPVTLSSIPVFQRGGTIVPRWMRVRSSSEC MKDDPITLFVALSPQGTAQGELFLDDGHT
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 ESRLSFQHDPETSVLVLRKPGINVASDWIHLR

SEQ ID No:208

MKLKLKNVFLAYFLVSIAGLLYALVQLGQPCDCLPPRLRAAAEQLRQKDLRISQLQAEIIRR
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 VSGLLAASGLLFTHLVVLTPKAQRLREGEPEGWVHPRGVEQRNKALDWLRGRGGAVGG
 EKDPPPPGTQGVVYFADDNTYSRELSEEMRWTRGVSVWPVGLVGGLRFEGPQVQD
 GRVVGFGHTAWEPSRPFPVDMAGFAVALPLLLDKPNAQFDSTAPRGHLESSLLSHLVDP
 KDLEPRAANCTRVLVWHTRTEPKMKQEEQLQRQGRGSDPAIEV

SEQ ID No:209

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 PDRMFVELSNSSWSEMSPWVIGTNYLYPMTPAIEQRLLQYLTPLGEYQELLPIFQLG
 SRELMMFYIDLKQTNDVLLTFEALKVKFLKILGHRGFFKNFVFFNLRWSLTSPRLECSG
 AILAHCNLRLLGSSDSPASASRVCVMHPNVLSDVVNYTLWLMECSHASGCCCHATMFFS
 ICFSFRAVLELFDRYDGLRRLVNLVSTLEILNLEDQGALLSDDEIFASRQTGKHTCMALR
 KYFEAHLAIKLEQVKQSLQRTEGGILVHPQPPYKACSYTHEQIVEMMEFLIEY GPAQLY
 WEPAEVFLKLSCVQLLQLISIACNWKTYYARNDTVRFALDVLAILTVPKIQLQLAESVD
 VLDEAGSTVSTVGISIILGVAEGEREFFIHDAEIQKSALQIIINCVCGPDRNISSIGKFISGTPRR
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 SPLIGRISFIRERPSPCNGRKIRVLRQKSDHGaySQSPAIIKKQLDRHLPSPTLDSIITEYL
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 HSQDRVIGTKGDIAHIYDIQTGNKLLTFNPDLANNYKRNCATFNPTDDLVLNDGVLDV

RSAQAIHKFDKFNMNISGVFHPNGLEVINTEWDLRTFHLLHTVPA LDQC R VVF NHTGT
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 LAVIENQGSMDALNMDTVCR LYEVGRQR LAEDEDEEEEDQEEEEQEEEDDDDEDDDDTD
 DLDELD TDQLLEAELEEDNNENAGEDGDNDFSPSDEELANLLEEGEDGEDEDSDADE
 EVELILGDTDSSDNSDLEDDIILSLNE

SEQ ID No:210

MASCPDSNDNSWLAGSESLPVETLGPA SRMDPESERALQAPHSPSKTDGKEAGTMD
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 PDTQDLEGQSPPQSLPSTPKAAWI REEGRCSSSSDDTDVMEGLRRRRGREAGPPQP
 MVPLAVENQAGGEGAGGELGISLNMC LL GALVLLGLGVLLFSGGLSESETGP MEEVER
 QVL PDPEVLEAVGDRQDGLREQLQAPVPPDSVPSLQNMGLL DKLAKENQDIRLLQAQ
 LQAQKEELQSLMHQPKGLEEENAQLRGALQQGEAFQRALESELQQLRARLQGLEADC
 VRGPDGVCLSGGRGPQGDKAIREQGPREQEPELSFLKQKEQLEAEAQALRQE LERQR
 RLLGSVQQDLERSLQDASRGDP A HAGLAE LGHRLA QKLQGLE NWGQDPGV SANASKA
 WHQKSHFQNSREWSGKEKWWDGQRDRKAEHWKHKKEESGRERKKNWGGQEDRE
 PAGR WKEGRPRV EESGSKKEGKRQGPKEPPRKSGSFHSSGEKQKQPRWREGTKDS
 HDPLPSWAELLRPKYRAPQGCSGVDECARQEGLTFGT ELAPVRQQELASLLRTYLAR
 LPWAGQLTKEPLSPAFFGEDGIFRHDRLRFRDFVDALEDSLEEVA VQQTGDDDEVDD
 FEDFIFSHFFGDKALKKRS GKKDKHSQSPRAAGPREGHSHHHHHHRG

SEQ ID No:211

AVPGADHGRQPAGNRRSIFSRTDLVRAGVLKEKPLWFDVYDAFPPLREP VFQRPRVR
 YGKAKAPIQDIWYHEDRIRAKFYSVYGS GQRAFDLFNPNF KSTCQRFV EKYTELQKLGE
 TDEEKLFVETGKALLAEGVILRRVGEQGLNTEVVTFPGNPNT

SEQ ID No:212

MRTLFNLLWLALACSPVHTTLSKSDAKKAASKT LLEKSQFS DKPVQDRGLV VTDLKAES
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 GREMFEVTGLHDVDQGWMRAVRKHAKGLHIVPRLLFEDW TYDDFRNVLDSEDEIEELS
 KTVVQVAKNQHFDGFVVEVWNQLLSQKRVGLIHMLTHLAEALHQARLL ALLVIPPAITPG
 TDQLGMFTHKEFEQLAPVLDGFSLMTYDYSTA HQPGPNAPLSWVRACVQVLDPKSKW
 RSKILLGLNFYGM DYATSKDAREPVVGARYI QT LKDHRPRMVWDSQASEHFFEYKKSR
 SGRHVVFYPTLKSLQVRLELARELG VGVSIWELGQGLDYFY DLL

SEQ ID No:213

MWIMTRTWGGQARVNGKIKAPARAGRTVSSCIFSSCLWFPLFRSSCLKTQPDSDACQP
ASPTRAAALPTRMGGTPPRCPRAERSRGSTGIARASALAAGGAGVLRGRDQSARAA
TPDLGRQLSSHCDGHWGAPSILVKFSL

SEQ ID No:214

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DIETRDCLQNTYNLNSVLAGVVCRSSHTDSVFLQCIQLLQKLTYNVKIFYSGANIDELITF
LIDHIQSSEDELKMPCLGLLANLCRHNLSVQTHIKTLSNVKSFYRTLITLLAHSSLTVVVFA
LSILSSLTNEEVGEKLFHARNIHQTFQLIFNILINGDGTLTRKYSVDLLMDLLKNPKIADYL
TRYEHFSSCLHQVLGLLNGKDPMSSSKVLELLLAFCSVTQLRHMLTQMMFEQSPPGSA
TLGSHTKCLEPTVALLRWLSQPLDGSENCVLALELFKEIFEDVIDAACNSSADRFTVLL
LPTILDQLQFTEQNLDEALTRKKCERIAKAIEVLLTCGDDTLKMHIAKILTTVKCTTLIEQQ
FTYKGIDLGFGTKVADSELCKLAADVILKTLDLINKLKPLVPGMEVSFYKILQDPRLITPLA
FALTSDNREQVQSGLRILLEAAPLPDFPALVLGESIAANNAYRQQETEHIPRKMPWQSS
NHSFPTSIKCLTPHLKGVPGLNIEELIEKLQSGMVVKDQICDVRISDIMDVYEMKLSTLA
SKESRLQDLLETKALALAQAQADRLIAQHRCQRTQAETEARTLASMLREVERKNEELSVLL
KAQQVESERAQSDIEHLFQHNRKLESVAEEHEILTKSYMELLQRNESTEKKNKDLQITC
DSLNUQIETVKKLNESLKEQNEKSIAQLIEKEEQRKEVQNQLVDREHKLANLHQKTKVQ
EEKIKTLQKEREDEKEETIDILRKELSRTEQIRKELSIKASSLEVQKAQLEGRLEEKESLVKL
QQEELNKHSHMIAMIHSLSGGKINPETVNLSI

SEQ ID No:215

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VYLGPLGNHWSGARIGKNNMATITISNDEDAPTIEEEAAYQVREPAGPDAIAILNIKVR
RGDQNRTSKVRCSTRDGSQAQSGVDYYPKSRVLKFSPGVDHIFFKVEILSNEDREWHE
FSLVLPDPVEAVLGDVTTATVTILDQEAAGSLILPAPPIVTLADYDHVEEVTKEGVKK
SPSPGYPLVCVTPCDPHFPRYAVMKERCSEAGINQTSVQFSWEVAAPTDNGAR~~N~~
ETITDNTPFTSVNHMVLDSIYFSRRFHVCVAKAVDKVGHVGTLRSNIVTIGTDSAICHT
PVVAGTSRGFQAQSFIATLKYL DVKHKEHPNRSGRWCLPPHID

SEQ ID No:216

RVYADAPAKLLLPPPAWDLAVRLRGAEAAASERQVYSVTMKLLLLHPAFQSCLLTLG
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 QHVQGHRLNSTCFSSGDLFTAHNFSEQSRIGSSELQEFCPTILQQQLDSRACTSENQEN
 EENEQTEEGRPSAVEVWGYGLLCVTVISLCSLLGASVVPFMKKTFYKRLLLFI
 AIGTLYSNALFQLIPEAFGFNPLEDYYVSKSAVVFGGFYLFFFTEKILKILLKQNEHHGHSHYA
 SESLPSKKDQEEGVMEKLQNGDLDHMIPQHCSELDGKAPMVDEKVIVGSLSVQDLQA
 SQSACYWLKGVRYSDIGTLAWMITLSDGLHNFDGLAIGASFTVSFQGISTSV
 AILCEEF PHELGDFVILLNAGMSIQQLFFNFLSACCCYLGLAGFILAGSHFSANWIFALAGGMFLYI
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SEQ ID No:217

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 EGVKK SPSPGYPLVCVTPCDPHPRYAVMKERCSEAGINQTSVQFSWEVAAP
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 VRCVAKAVDKVGHVG
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 DRNQPEV
 TDKYFHD
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SEQ ID No:218

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FFSWHTPLACEQATECSV RNGSSIVDLSPLI HRTGGYEAYDESEDDASDTNPDFYINIC
QPLNPMHAVPCPAGAAVCKVPIDGPPIDIGRVAGPPI LNP IANEIYLN FESSTPCLADKH
NYTS LIAFHCKRGVSMGTPKLLRTSECDFVFEWETPVVCPDEV RMDG CTL DEQLL
FN LSSLSTSTFKVTRDSRTYSVGCTFAVGPEQGGCKDGGVCLLSGTKGASFGRLQS
MKLDYRHQDEAVVLSYVNGDRCP PETDDGVPCVFPFIFNGKSYEECIIESRAKLWCSTT
ADYDRDHEWGFCRHSNSY RTSSIIFKCDEDEDIGRPQVFSEVRGCDVT FEWKT
PKKLECKFVQKHKT YDLRLLSSLTGSWSLVHNGVSYYINLCQKIYKGPLGC SERASICR
RTTG DVQVLGLVHTQKLGVIGDKVVVTYSKGYP CGGNKTASSVIELTCTKTVGRPAFK

RFDIDSCTYYFSWDSRAACAVKPQEVMVNGTITNPINGKSFSLGDIYFKLFRASGDMRTNGDNYLYEIQLSSITSSRNPACSGANICQVKPNDQHFSRKVGTSDFKTKYLYQDGDLDVVFASSSKCGDKTKSVSSTIFFHCDPLVEDGIPEFSHETADCQYLFWSWYTSAVCPLGVGFDSENPGGQMHKGLSERSQAVGAVLSLLVALTCCLALLLYKKERRETVISKLTCCRSSNVSYKYSKVNEEETDENETEWMEEIQLPPPRQGKEGQENGHITTKSVKALSSLHGDDQDSEDEVLTIPENVHSGRGAGAESSHPVRNAQSNALQEREEDDRVGLVRGEKARKGKSSSAQQKTVSSTKLVSFHDDSDEDLLHI

SEQ ID No:219

MAFPPIRRRLRGPRGLPLLSGLLPLCRAFNLDVDSPAEGSGPEGSYFGFAVDFFVPSASSRMFLVGAPKANTTQPGIVEGGQVLKCDWSSTRRCQIEFDATGNRDYAKDDPLEFKSHQWFGASVRSKQDKILACAPLYHWRTREMQEREPVGTCFLQDGTKTVEYAPCRSQDIDADGQGFCQGGFSIDFTKADRVLGGPGSFYWQGQLISDQVAEIVSKYDPNVYSIKYNNQLATRTAQAFDDSYLGYSAVGDFNGDGIDDFVSGVPRAARTLGMVYIYDGKNMSSLYNFTGEQMAAYFGFSVAATDINGDDYADVFIGAPLFMDRGSDGKLQEVGQSVSLQRASGDFQTTKNGFEVFARFGSAIAPLGDLDDQDGFDIAIAAPYGGEDKKGIVYIFNGRSTGLNAVPSQILEGQWAARSMPSPSGYSMKGATDIDKNGYPDLIVGAFGVDRAILYRARPVITVNAGLEVYPSILNQDNKTCSLPGTALKVSCFNRFCCLKADGKGVLPRKLNQVELLDKLIKQKGAIRRRLFLYSRSPSHSKNMTISRGGLMQCEELIAYLRDESEFRDKLTPITFMEYRLDYRTAADTTGLQPILNQFTPANISRQAHILLDCEDNVCKPKLEVSVDSDQKKIYIGDDNPLTLIVKAQNQGEGAYEAELIVSIPLQADFIGVVRNNEALARLSCAFKTENQTRQVVCDLGNPMKAGTQLLLAGLRFVHQQSEMDTSVKFDLQIQSSNLFDKVSPVVSHKVDLAVLAAVEIRGVSSPDHIFLPIPWEHKENPETEEDVGPVVQHIYELRNNGPSSFSKAMILHLQWPYKYNNTLLYLHYDIDGPMNCTSDEINPLRIKISSLQTTEKNDTVAGQGERDHЛИKRDALSEGDIHTLGCVAQCLKIVCQVGRDRGKSAILYVKSLLWTETFMNKENQNSYSLKSSASFNVIEFPYKNLPIEDITNSTLVTTNVTWGIQPAPMPVPVVIIAVLAGLLLALVFVMYRMGFFKRVPPQEEQEREQLQPHENGEGNSET

SEQ ID No:220

MTEKMSSFLYIGDIVSLYAEGSVNGFISTLGLVDDRCVVHPEAGDLANPPKKFRDCLFKVCPMNRYSAQKQYWAKQAKQGNHTEAALLKKLQHAAELEQKQNESENKKLLGEIVKYSNVIQLLHIKSNKYLTVNKRLPALLEKNAMRVSLDAAGNEGWSFYIHPFWKLSEGDNIVVGDKVVLMPVNAGQPLHASNIELLDNPGCKEVNAVNCNTSWKITLMKYSSYREDVLKGGDVVRLFHAEQEKFLLTCDEYEKKQHIFLRTTLRQSATSATSSKALWEIEVVHHDPCRG

GAGQWNSLFRFKHLATGNYLAAELNPDYRDAQNEGKNVRDGVPPTSKKKRQAGEKIM
YTLVSVPHGNDIASLFELDATTLQRADCLVPRNSYVRLRHLCTNTWVTSTSIPIDTDEER
PVMLKIGTCQTKEAFAIVSPLSEVRDLDFANDANKVLATTVKLENGTITQNERRF
VTKLLEDLIFFADVPNNGQEVLVVITKPNRERQKLMREQNILAQVFGILKAPFKEKAG
EGSMLRLEDLGDQRYAPYKYMRLCYRVLRHSQQDYLKNQEYIAKNFCVMQSQIGYDI
LAEDTITPLLHNNRKLEKHITAKEIETFVSSLRRNREPRFLDYLSDLCVSNTTAIPVTQELI
CKFMLSPGNADILIQTKVVSMQADNPMESSILSDDIDEVWLYWIDSNEPHGKAIRHL
AQEAKEGTkadlevltyryqlnlfarmcldrqlainqistqlsvdlilrcvsdeslpf
DLRASFRCRLMLHMHVDRDPQESVVPVRYARLWTEIPTKITIHEYDSITDSSRNDMKRKF
ALTMEFVEEYLKEVVNQPFPFDKEKNKLTFEVVLARNLIYFGFYSFSELLRLTRTLLAI
LDIVQAPMSSYFERLSKFQDGNNVMRTIHGVGEMMTQMVLRSGSIFPMSPDVPPSI
HPSKQGSPTEHEDVTMDTKLIIIEILQFILSVRLDYRISYMLSUYKKEFGEDNDNAETSA
SGSPDTLLPSAIVPDIDEIAAQAEATMFAGRKEKNPVLQLDDEGGRTFLRVLIHLIMHDYAPL
LSGALQLLFKHFSQRAEVLQAFKQVQLLVSNQDVDNYKQIKADLDQLRLTVEKSELWVE
KSSNYENGEIGESQVKGGEEPIEESNILSPVQDGTKKPQIDSNSNKYRIVKEILIRLSKL
CVQNKCRNQHQRLLNMGAHSSVVLQDLLQIPYEKNDEKMNEVMNLATHFLQNFCRGN
PQNQVLLHKHNLFLTPGLLEAETMRHIFMNNYHLCNEISERVVQHFVHCIETHGRHVE
YLRFLQTIVKADGKYVKKCQDMVMTELINGGEDVLIFYNDRASFPILLHMMCSERDRGD
ESGPLAYHITLVELLAACTEGKNVYTEIKCNSLLPLDDIVRVVTHDDCIPEVKIAYVNFnH
CYVDTEVEMKEIYTSNHIWKLFENFLVDMARVCNTTDRKHADIFLEKCVTESIMNIVSG
FFNSPFSDNSTSLQTHQPVFIQLLQSAFRIYNCTWPNPAQKASVESCIRTLAEVAKNRGI
AIPVDLDSQVNTLFMKSHSNMVQRAAMGWRLSARSGPRFKEALGGPAWDYRNIIEKLQ
DVVASLEHQFSPMMQAEFSVLVDVLYSPELLFPEGSDARIRCAGAFMSKLINHTKCLMEK
EEKLCIKILQTLREMLEKKDSFVEEGNTLRKILLNRYFKGDYSIGVNGHLSGAYSKTAQV
GGSFSGQDSDKMGISMDSIQCLLDKEGASELVIDVIVNTKNDRIFSEGIFLGIALLEGNT
QTQYSFYQLHEQKKSEKFFKVLYDRMKAQKEIRSTVTVNTIDLGNKKRDDDNEELMT
SGPRMRVRDSTLHLKEGMKGQLTEASSATSKAYCVRREMDPEIDIMCTGPEAGNTEE
KSAEEVTMSPAIAIMQPIRLFLQLLCENHNRELQNFLRNQNNKTNYNLVCETLQFLDCIC
GSTTGGGLLLGLYINEKNVALVNQNLESLTEYCQGPCHENQTCIATHESNGIDIIIALLND
INPLGKYRMDLVLQLKNNASKLLAIMESEHDSENAERILFNMRPRELVDVMKNAYNQG
LECDHGDDDEGGDDGVSPKDVGHNIYILAHQLARHNKLQQMLKPGSDPDEGDEALKYY
ANHTAQIEIVRHDRTEQIVFPVPNICEYLTRESKCRVFNTTERDEQGSKVNDFFQQTE
DLYNEMKWQKKIRNNPALFWFSRHISLWGSISFNLAVALFYPFGDDGDEGTLS
PLFSVLLWIAVAICTSMLFFFSKPVGIRPFLVSIMLRSIYTIGLGPLILLGAANLCNKIVFLV

SFVGNRGTFTRGYRAVILDMAFLYHVAYVLVCMGLFVHEFFYSFLLFDLVYREETLLNV
 IKSVRTNNGRSILTAVLALILVYLFSIIGFLFLKDDFTMEVDRLNRTPTGSHQVPTMTLTT
 MMEACAKENCSPTIPASNTADEEYEDGIERTCDTLLMCIVTVLNQGLRNGGVGDVLR
 RPSKDEPLFAARVVYDLLFYFIVIIIVLNLIIFGVIIDTFADLRSEKQKKEEILKTCFCIGLER
 DKFDNKTVSFEEHIKSEHNMWHYLYFIVLVKVKDPTEYTGPESYVAQMIVEKNLDWFPR
 MRAMSLVSNEGDSEQNEIRSLQEKLESTMSLVKQLSGQLAELKEQMTEQRKNKQRLG
 FLGSNTPHVNHMPPH

SEQ ID No:221

MVSSGCRMRSLWFIIVISFLPNTEGFSRAALPFGLVRRELSCEGYSIDLRCPGSDVIMIES
 ANYGRTDDKICDADPFQMENTDCYLPDAFKIMTQRCNNRTQCIVVTGSDVFDPDCPGT
 YKYLEVQYECVPYIFVCPGTLKAIVDSPCIYEAEQKAGAWCKDPLQAADKIYFMPWTPY
 RTDTLIEYASLEDFQNSRQTTYKLPNRVDGTGFVYDGAVFFNKERTRNIVKFDLRTRI
 KSGEAIINYANYHDTSPYRWGGKTDIDLAVDENGLWVIYATEQNNGMIVISQLNPYTLRF
 EATWETVYDKRAASNAFMICGVLYVVRVSYQDNESETGKNSIDYIYNTRLNRGEYVDVP
 FPNQYQYIAAVDYNPRDNQLYVWNNNFILRYSLEFGPPDPAQVPTTAVTITSSAELFKTII
 STTSTSQKGPMSTTVAGSQEGSKGTKPPPASSTKIPPITNIFPLPERFCEALDSKGK
 WPQTQRGMMVERPCPKGTRGTASYLCMISTGTWNPKGPDLSNCTSHWVNQLAQKIR
 SGENAASLANELAKHTKGPVFAGDVSSVRLMEQLVDILDAQLQELKPSEKDSAGR SY
 NKAIVDTVDNLLRPEALESWKHMNSSEQAHTATMLLDTLEEGAFVLADNLLEPTRVSMP
 TENIVLEVAVLSTEGQIQDFKFPLGIKGAGSSIQLSANTVKQNSRNGLAKLVFIYRSLGQ
 FLSTENATIKLGADFIGRNSTIAVNSHVISVSINKESSRVYLTDPVLFTLPHIDPDNYFNAN
 CSFWNYSERTMMGYWSTQGCKLVDTNKTRTTCACSHLTNFAILMAHREIAYKDGVHEL
 LLTVITWVGIVISLVCLAI CIFTFCFFRGLQSDRNTIHKNLCINLFIAEFIFLIGIDKTKYAIACP
 IFAGLLHFFFIAFAWMCLEGVQQLYMLVEVFESEYSRKYYYYVAGYLFPATVVGVSAAI
 DYKSYGTEKACWLHVDNYFIWSFIGPVTIILLNIIFLVITLCKMVKHSNTLKPDSSRLENIK
 SWVLGAFALLCLLGLTWSFGLLFINEETIVMAYLFTIFNAFQGVFIFIFHCALQKKVRKEY
 GKCFRHYSYCCGGLPTESPHSSVKASTRTSARYSSGTQSRIRRMWNDTVRKQSESSFI
 SGDINSTSTLNQGHSLNNARDTSAMDTPLNGNFNNNSYSLHKGDYNDSVQVVDGGLSL
 NDTAFEKMIISELVHNNLRGSSKTHNLELTPVKPVIGGSSSEDDAIVADASSLMHSDNP
 GLELHHKELEAPLIPQORTHSLLYQPQKKVKSEGTD SYVSQQLTAEAEEDHLQSPNRDSL YT
 SMPNLRDSPYPESSPDMEEDLSPSRRSENE DIYYKSMPNLGAGHQLQMCYQISRGNS
 DGYIIPINKEGCPEGDVREGQMQLVTS L

SEQ ID No:222

MRLTRCQAALAAAITLENLLVLFYVSWLQHQPRNSRARGPAAAGPRVTVLVREFEA
 FDNAVPELVDSFLQQDPAQPVVVAADTLPPPLALPRIPNVRLALLQPALDRPAAASRP
 ETYVATEFVALVPDGARAEEAPGLLERMVEALRAGSARLVAAPVATANPARCLALNVSLR
 EWTARYGAAPAAPRCDAFDGDAVLLRARDLFNLSAPLARPGTSLFLQTAALRGWAVQ
 LLDLTFAAARQPPLATAHARWKAEREGRARRAALLRALGIRLVSWEGGRLEWFGCNKE
 TTRCFGTVVGDTPAYLYEERWTPPCCLRALRETARYVVGVLAAAGVRYWLEGGSLLGA
 ARHGDIIPWDYDVLGIYLEDVGNCEQLRGAEAGSVVDERGFVWEKAVEGDFFRVQYS
 ESNHLHVDLWPFYPRNGVMTKDTWLDHRQDVEFPEHFLQPLVPLFAGFVAQAPNNY
 RRFLELKFGPGVIENPQYPNPALLSLTGSG

SEQ ID No:223

MPRGQKSCLRAREKRQRTRGQTQDLKVGQPTAAEKEESPSSSSVLRDTASSSLAFGI
 PQEPQREPPSTSAAAAMSCGSDKGDESQDEENASSSQASTSTERSLKDSLTRKTKM
 LVQFLKYKMKETTKAEMLKIISKKYKEHFPEIFRKVSQRTELVFGLALKEVNPTTHSY
 ILVSMGPNDGNQSSAWTLPRNGLMLPLSVIFLNGNCAREEEIWEFLNMLGIYDGKRH
 LIFGEPRKLITQDLVQEKEYQQVPNSDPPRYQFLWGPRHAETSKMKVLEFLAKVND
 TTPNNFPLLYEEALRDEEERAGARPRVAARRGTTAMTSAYSRATSSSSQPM

SEQ ID No:224

MTLIEVGDEVTLFSVLACLLVLALAWVSTHTAEKKDPLQPSPGTPTPSQPSAAMAAT
 DSMRGEAPGAETPSLRHRGQAAQPEPSTGFTATPPAPDSPQEPLVRLKFLNDSEQVA
 RAWPHDTIGSLKRTQFPGREQQVRLIYQQQLLGDDTQTLGSLHLPPNCVLHCHVSTRV
 GPPNPPCPGSEPGPSGLEIGSLLLPLLLLLLWYCQIQYRPFFPLTATLGLAGFTLLL
 SLLAFAMYRP

SEQ ID No:225

MVVALRYWWPLLCSPLLIQIPEEYEGHHVMEPPVITEQSPRRLVVFPTDDISLKCEAS
 GKPEVQFRWTRDGVHFKPKEELGTVYQSPHSGSFTITGNNNSNFAQRFQGIYRCFASN
 KLGTAAMSHEIRLMAEGAPKWPKETVKPVEEESVVLPCNPPPSAEPLRIYWMNSKIL
 HIKQDERVTMGQNGNLYFANVLTSDNHSDYICHAFPGTRTIIQKEPIDLRVKATNSMID
 RKPRLLFPTNSSSHLVALQQQPLVLECIAEGFPTPTIKWLRLPSGPMPADRVTYQNHNK
 LQLLKVGEEEDDGEYRCLAENSLGSARHAYYVTVEAAPYWLHKPQSHLYGPGETARLDC
 QVQGRPQPEVTWRINGIPVEELAKDQKYRIQRGALILSNVQPSDTMVTQCEARNRHGL

LLANAYIYVQLPAKILTADNQTYMAVQGSTAYLLCKAFGAPVPSVQWLDEDGTTVLQD
 ERFFPYANGTLGIRDLQANDTGRYFCLAANDQNNVTIMANLKVKDATQITQGPRSTIEKK
 GSRTFTCQASFDPQLQPSITWRGDGRDLQELGDSDKYFIEDGRLVIHSLDYSQGNY
 SCVASTELDVVESRAQLLVVGSPGPVPRLVSDLHLLTQSQRVWSSPAEDHNAPIEKY
 DIEFEDKEMAPEKWYSLGKVPGNQTSTTLKLSPYVHYTFRVTAINKYGPGEPSPVSETV
 VTPEAAPEKNPVDVKGEGNETTNMVITWKPLRWMDWNAPQVQYRVQWRPQGTRGP
 WQEIQIVSDPFLVVSNTSTFV PYEIKVQAVNSQKGPEPQVTIGYSGEDYPQAIPLEGIE
 ILNSSAVLVKWRPVDLAQVKGHLRGYNVTWREGSQRKHSKRHIHKDHVVVPANTTSV
 ILSGLRPYSSYHLEVQAFNGRGSGPASEFTFSTPEGVPGHPEALHLECQSNTSLLRW
 QPPLSHNGVLTGYVLSYHPLDEGGKGQLSFNLRDPELRTHNLTDSPHLRYRFQLQAT
 TKEGPGEAIVREGGTMALSGISDFGNISATAGENYSVSVWPKEGQCNRFHILFKALG
 EEKGGASLSPQVSYNQSSYTQWDLQPDTDYIEHLFKERMFRHQMAVKTNGTGRVRL
 PPAGFATEGWFIGFVSAILLLLVLLILCFIKRSKGGKYSVKDKEDTQVDSEARPMKDET
 GEYRSLESDNEEKAFGSSQPSLNGDIKPLGSDDSLADYGGSDVQFNEDGSFIGQYSG
 KKEKEAAGGNDSSGATSPINPAALE

SEQ ID No:226

MAVAVRTLQEQUEKAKESLKNVDENIRKLTGRDPNDVRPIQARLLALSGPGGGRRGRGS
 LLLRRGFSDGGGPPAKQRDLEGAVSRLGGERRRRESRQESDPEDDDVKKPALQSS
 VVATSKERTRRDLIQDQNMDEKGKQRNRRIFGLLMGTQKFKQUESTVATERQKRRQE
 EQKLEVQAEEERKVENERRELFEERRAKQTELRLLEQKVELAQLQEEWNEHNAKIKY
 IRTKTKPHLFYIPGRMCPATQKLIIESQRKMNALFEGRIEFAEQINKMEARPQQSMKE
 KEHQVVRNEEQKAEQEEGKVAQREEELEETGNQHNDVEIEEAGEEEEKEIAIVHSDAE
 KEQEEEEQKQEMEVKMEETEVRESEKQQDSQPEEVMDVLEMVENVKHVIADQEVME
 TNRVESVEPSENNEASKELEPEMEFEIEPDKECKSLSPGKENVSALDMEKESEEKEKES
 EPQPEPVAQPQPQSQPQLQLQSQSQPVLQSQQPSQPEDLSAVLQPTPQVTQEKGHL
 LPERKDFPVESVKLTEVPVEPVLTVPESKSKTTRSRGRARNKTSRSRSSSSSS
 SSSSTSSSSGSSSSGSSSSRSSSSSSSTGSSGRDSSSTSSSESRSRSRGRG
 HNRDRKHRRSVDRKRRDTSGLERSHKSSKGSSRDTKGSKDKNSRSDRKRSISESSR
 SGKRSR SERDRKSDRKDKRR

SEQ ID No:227

MLRLSERNMKVLLAAALIAGSVFFLLPGPSADEKKKGPKVTVKVFDLRIGDEDVGRV
 IFGLFGKTVPKTVDNFVALATGEKGFGYKNSKFHRVIKDFMIQGGDFTRGDGTGGKSIY

GERFPDENFKLKHYGPGWVSMANAGKDTNGSQFFITTVKTAWLDGKHVVFGKVLEGM
EVVRKVESTKTDSDRKPLKDVIADCGKIEVEKPFIAKE

SEQ ID No:228

MASCVGSRTL SKDDVNYKMHFRMINEQQVEDITIDFFYR PHTITLLSFTIVSLMYFAFTRD
DSVPEDNIWRGILSVIFFFLIISVLA FPNGPFTRPHPALWRMVFG LSVLYFLFLVFLLFLNF
EQVKSLMYWLDPNLRYATREADVM EYAVNCHVITWERIISHFDIFAFGHFWGWAMKAL
LIRSYGLCWTISITWELTELFM HLLPNFAECWW DQVILDILL CNGGGIWLGMVVCRFLE
MRTYHWASFKDIHTTGKIKRAVLQFTPASWTYVRWFDPKSSFQRVAGVYLFMIWQLT
ELNTFFLKHFV FQASHPLSWGRILFIGGITAPTVRQYYAYLTDTQCKRVGTQCWVFGVI
GFLEAIVCIKFGQDLFSKTQILYVVLWLLCVAFTTFLCLYGMIWYAEHYGHREKTYSECE
DGTY SPEISWHHRKG KGSED SPPK HAGNNESHSSRRRN RHSKS KVTNGVGKK

SEQ ID No:229

MAEAKTHWLGAALSLIPLFLISGAE AASFQRNQLLQKEPDLRLEN VQKFPSPE MIRALE
YIENLRQQAHKEESSPDYNPYQGVSVPLQQKENGDESHLPERDSLSEEDWMRIILEAL
RQAENE PQSAPKENKP YALN SEKNFPMDMSDDYETQQWPERKLKHMQFPPMYEENS
RDNP FKRTNE IVEEQYTPQSLATLESV FQELGKLTGPNNQKRERMDEE QKLYT DDED
YKANNIAYEDVVGGEDWNPVEEKIESQTQEEVRDSKENIGKNEQINDEM KRSGQLGIQ
EEDLRKESKDQLSDDVSKVIA YLKRLVNAAGSGRLQNGQNGERATRLFEKPLDSQS
LIEISRNLQIPP EDLIEMLK TGEKPNGSVE PERELDLPVDL DISEADLDHPDLFQNRMLS
KSGYPKTPGRAGTEALPDGLSVEDILNLLGMESAANQKTSYFPNPYNQE KVLPRLPYG
AGR SRSNQLPKAAWIPHVENRQMAYENLNDKDQELGEYLARMLV KYPEIINSNQVKRV
PGQGSSEDDLQEEEQIEQAIKEHLNQGSSQETDKLAPVSKRFPVGPPKND DTPNRQY
WDEDLLMKVLEYLNQEKAEGREHIAKRAMENM

SEQ ID No:230

MAVVKNKCLMKGGKKGVKKIIDPFSKKDQKYW KDLVTR TQGTQIASDGLKGLVFEVSL
ADVQNDEVAFRKLKLITEDVQGKNCLTFYGMGLSCDKICSMFENCSTMIEAHVDVKTT
DDNIGKDVEKACQFILSMSL EKGREFQHHFWPLKKAATIRMSSPHVTISRDSKEEGN
KAASSHYSRGGA KYEGEAVKRS LVE SYTHPNSKETERRENIDTVLNWFTKEEFDFTLY
YREPDMGHRFRPEAENRKLMIQQINRTIGPWDDHREEETQCQQDPLSNYIKFRDCVK
FDIVGYGGFGMPLTKLGQEEALYQALKNVHPDLHVYKKEFPEDFHLAKHDQVLPI
NCGYSINGRIIMCFNKGSHGFDNVLMDIKTIFRDFGPDFKRNRLAEPFNSIHIYPFVSPGS

HPQTHINGSLAVTQEMLMSSYDQQPGGRRGERRGPQGSRESRGRRDGSPCRSPRHA
 RHGEITQRFANTFYCVNVPVNAPLRFLSLPSTQSLEAKLTDSSDSELLRDILQKTVKHP
 VCVTHPPSVKYARCFLSELIKKEAVHTEPLDELYEVLVETLMAKESTQGHWSYLLDCP
 RAWQWCWPHSPGHLQDVPPPGIHLQRLSQPGPQTAPRECPSQWPLIRGRHHCQLSP
 RVTVAQLDWDIAMVHQLSAIQPDVVIADVLYCPEAIVLLVGVLLRLAACREHQRAPEVY
 VAFTVRNPETCQLFTTELGQARIRWEVEPRHDQKLFPYEEHLEMAMLNLTL

SEQ ID No:231

MSSQPAGNQTSPGATEDYSYGSWYIDEPQGGEELQPEGEVPSCHTSIPPGLYHACLA
 SLSILVLLLLAMLVRRRQLWPDCVRGRPGLPSPVDFLAGDRPRAVPAAVFMVLLSSLCL
 LLPDEDALPFLTASAPSQDGKTEAPRGAWKILGLFYYAALYYPLAACATAGHTAAHLLG
 STLSWAHLGVQVWQRAECPVQPKIYKYYSLASLPLLLGLGFLSLWYPVQLVRSFSRRT
 GAGSKGLQSSYSEEYLRNLLCRKKLGSSYHTSKHGFLSWARVCLRHCIYTPQPGFHLP
 LKLVLSATLTGTAIYQVALLLLGVVPTIQKVAGVTTDVSYLLASFGIVLSEDKQEVELV
 KHHLWALEVCYISALVSLCLTFVLMRSLVTHRNLRALHARGAALDLSPHRSPHPSRQ
 AIFCWMSFSAYQTAFICLGLLVQQIIFFLGTTALAFVLMPVLHGRNLLLFRSLESSWPFW
 LTALALAVILQNMAAHWFLETHDHPQLTNRRVLYAATFLLFPLNVLVGAMVATWRVLL
 SALYNIAIHLGQMDLSLLPPRAATLDPGYYTYRNFLKIEVSQSHPAMTAFCSSLQAQSL
 PRTMAAPQDSLRLPGEEDEGMQLLQTKDSMAKGARPGASRGRARWGLAYTLLHNPTL
 QVFRKTALLGANGAQP

SEQ ID No:232

GTRGPPGSPPPPPVRGMPGCPGCPGCGMAGRPLLFLTALALELLGRAGGSQPALRSR
 GTATACRLDNKESESWGALLSGERLDTWICSLLGSLMVGLSGVFPLLVIPLEMGTMLRS
 EAGAWRLKQLLSFALGGLLGNVFLHLLPEAWAYTCASPGGEGQSQLQQQLGLWVI
 AGILTFLALEKMFLDSKEEGTSQAPNKDPTAAAAALNGGHCLAQPAAEPLGLGAVVRSIK
 VSGYNLLANTIDNFTHGLAVAASFVSKKIGLLTTMAILHEIPHEVGDFAILLAGFDRW
 SAAKLQLSTALGGLLGAGFAICTQSPKGVVGCSPAEEETAAWVLPFTSGGFLYIALVNL
 PDLLEEDPWRSLLQQLLLLCAGIVVMVLFLSFVD

SEQ ID No:233

MAERRRHKKRIQEVGEPSSKEEKAVAKYLRFCPTKSTNMGMHRVDYFIASKAVDCLLD
 SKWAKAKKGEEARFTTRESVVDYCNRLLKKQFFHRALKVMKMKYDKDIKKEKDKGKAE
 SGKEEDKKSKKENIKDEKTKEKEKEKKDGEKEESKKEETPGTPKKKETKKKFLEPHDD

QVFLDGNEVYVWIYDPVHFKTFVMGLILVIAVIAATLFPLWPAEMRVGVYYLSVGAGCFV
 ASILLAVARCILFLIIWLITGGRHHFWFLPNLTADVGFIIDSFRPLYTHEYKGPKADLKKDE
 KSETKKQQKSDSEEKSDSEKKEDEEGKVGPGNHGTEGGGERHSDTDSDRREDDRS
 QHSSNGNDFEMITKEELEQQTDGDCEEDEEEENDGETPKSSHEKS

SEQ ID No:234

MAAEGWIWRWGWRRCGLRPGLLGPGPPTPLFLLLLGSVTADITDGNSEHLKRE
 HSLIKPYQGVGSSSMPDWDFQGSTMLTSQYVRLTPDERSKEGSIWNHQPCFLKDWE
 HVHFKVHGTGKKNLHGDGIALWYTRDRLVPGPVFGSKDNFHGLAIFLDTYPNDETTER
 VFPYISVMVNNGSLSYDHSKDGRWTELAGCTADFRNRDHDTFLAVRYSRGRLTVMTDL
 EDKNEWKNCIDITGVRLPTGYYFGASAGTGDLSDNHDISMKLFQLMVEHTPDEESIDW
 TKIEPSVNFLKSPKDNVDDPTGNFRSGPLTGWRVFLLLALLGIVVCAVVGAVVFQKR
 QERNKRFY

SEQ ID No:235

MDSNTAPLGSCPQPPPAPQPQARSRLNATASLEQERSERPRAPGPQAGPGPGVRD
 AAAPAEPAQHQHRSRERADGTGPTKGDMIEIPFEEVLERAKAGDPKAQTEVGKHYLQLA
 GDTDEELNSCTAVDWLVLAAKQGRREAVKLLRRCLADRRGITSENEREVRQLSSETDL
 ERAVRKAALVMYWKLNPKKKQVAVAELLENVGQVNEHDGGAQPGPVPKSLQKQRR
 MLERLVSSESKNYIALDDFVEITKKYAKGVIPSSLFLQDDDEDDDELAGKSPEDLPLRLKV
 VKYPLHAIMEIKEYLIDMASRAGMHWLSTIIPTHHINALIFFFIISNLTIDFFAFFIPLVIFYLSF
 ISMVICTLKVFQDSKAWENFRTLTDLLRFEPNLDVEQAEVNFGWNHLEPYAHFLLSVFF
 VIFSFPIASKDCIPCSSELAVITGFFTTSYLSLSTHAEPYTRRALATEVTAGLLSLLPSMPL
 NWPYLKVLGQTFITVPVGHLVVLNVSPCULLYVYLLYLFFRMAQLRNFKGTYCYLVPYLV
 CFMWCELSVVILLESTGLGLRASIGYFLFLPALPILVAGLALVGVLQFARWFTSLELTKIA
 VTVAVCSVPLLRWWTKASFVVGVMVKSLTRSSMVKLILVWLTAIVLFCWFYVYRSEGM
 KVYNSTLTWQQYGYALCGPRAWKETNMARTQILCSHLEGHRWTGRFKYVRTDIDN
 SAESAINMLPFIGDWMRCLYGEAYPACSPGNTSTAEEELCRLKLLAKHPCHIKKFDRY
 KFEITVGMPFSSGADGSRSREEDVTKDIVLRASEFKSVLLSRQGSLIEFSTILEGRLG
 SKWPVFELKAISCLNCMAQLSPTRRHVKIEHDWRSTVHGAVKFAFDFFFFPFLSAA

SEQ ID No:236

MNNQKQQKPTLSGQRFKTRKRDEKERFDPTQFQDCIIQGLTETGTDLEAVAKFLDASG
 AKLDYRRYAETLFDILVAGGMLAPGGTLADDMMRTDVCVFAAQEDLETMQAFQAQVFNK

LIRRKYKYLEKGFEDEVKKLLLFLKGFSESERNKLAMLTGVLLANGTLNASILNSLYNENLV
 KEGVSAAFAVKLFKSWINEKDINAVAASLRKVSMNDNRLMELFPANKQSVEHFTKYFTEA
 GLKELSEYVRNQQTIGARKELKQELQEQQMSRGDPFKDIILYVKEEMKKNNIPEPVVIGIV
 WSSVMSTVEWNKKEELVAEQAIKHLQYSPLLAFTTQQQSELLLLKIQEYCYDNIHF
 MKAFQKIVVLFYKAEVLSSEPILKWYKDAHVAKGKSVFLEQMKKFVEWLKNAEEESESE
 AEEGD

SEQ ID No:237

MENHKSNNKENITIVDISRKinQLPEAERNLLENGSVYVGLNAALCGLIANSLFRRILNVT
 KARIAAGLP MAGIPFLTTDLTYRCFVSFPLNTGDDCETCTIRSGLTGLVIGGLYPVFLAI
 PVNGGLAARYQSALLPHKGNILSYWIRTSKPVFRKMLFPILLQTMFSAVLGSEQYKLLIK
 ALQLSEPGKEIH

SEQ ID No:238

MGDILAHESELLGLVKEYLDFAEFEDTLKTFSKCKIKGKPLCKTVGGSFRDSKSLTIQK
 DLVAADFNGDQKVFFDLWEEHISSSI RDGDSFAQKLEFYLHIHFAIYLLKYSVGRPDKEE
 LDEKISYFKTyleTKGAALSQTTEFLPFYALPFVPNPMVHPSFKELFQDSWTPELKLKE
 KFLALISKASNTPKLLTIYKENGQSNKEILQQLHQQLVEAERRSVTYLKRYNKIQADYHNL
 IGVTAELVDSLEATVSGKMITPEYLQSVCVRLFSNQMRQSLAHSDFTRPGTASTMLRA
 SLAPVKLKDVPPLLPSLDYEKLKKDLILGSDRLKAFLLQALRWRLTSHPGEQRETVLQAY
 ISNDLLDCYSHNQRSQLQLLHSTDVVRQYMARLINAFAASLAEGRLYLAQNTKVLQMLE
 GRLKEEDKDIITRENVPGALQKFSLRRPLQTAMIQDGLIFWLVDVLKDPCCLS DYTLEY
 VALLMNLCRSTGKNMCAKVAGLVLKVLS DLLGHENHEIQPYVNGALYSILSVP SIREEA
 RAMGMEDILRCFIKEGNAEMIRQIEFIKQLNSEELPDGVLESDDDEDDEDDEEDHDIMEA
 DLDKDELIQPQLGELS GEKLLTEYLGIMTNTGKTRRKGLANVQWSGDEPLQRPVTPG
 GHRNGYPV

SEQ ID No:239

IATVIVITVMLKKKQYTSIHHGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN

SEQ ID No:240

MSAGSERGAAATPGGLPAPCASKVELRLSCRHLLDRDPLTKSDPSVALLQQAQGQWV
 QVGRTEVVRSSLHPVFSKVFTVDYYFEEVQRLRFEVYDTHGPSGFSCQEDDFLGGME
 CTLGQPAQKWLLQVVMRVSVDLGPAGHCAKHFLCCTESSHLARTGPSFLLRYDDLCL

PWATAGAVRWWTCRGGHTQGWQIVAQKKVTRPLLLKFGRNAGKSTITVIAEDISGNNG
 YVELSFRARKLDDKDLFSKSDPFLELYRVNDDQGLQLVYRTEVVKNLNPVWEAFKVS
 LSSLCSCEETRPLKCLWDYDSRGKHDFIGEFSTTFEEMQKAFEEGQAQWDCVNPKY
 KQKRRSYKNSGVVLADLKHFHRVYSFLDYIMGGCQIHFTVAIDFTASNGDPRNSCSLHYI
 NPYQPNEYLKALVSVEICQDYDSDKRFSALGFGARIPPKYEVSHDFAINFNPEDDECE
 GIQGVVEAYQNCLPRVQLYGPTNVAPIISKVARVAAAESTGKASQYYILLTDGVVTD
 MADTREAIVRASRLPMSIIIVGVGNADFTDMQVLDGDDGVLRSRGEPALRDIVQFVPF
 RELKNASPAALAKCVLAEVPKQVVEYYSHRGLPPRSLGVPAGEASPGCTP

SEQ ID No:241

MAACQCVTKVALNVSCANLLKDIGSKSDPLCVLFLNTSGQQWYEVERTERIKNCLNPQF
 SKTFIIDYYFEVVQKLKFGVYDIDNKTIELSDDDFLGECECTLGQIVSSKKLTRPLVMKTG
 RPAGKGSITISAEEIKDNRVVLFEMEARLKLDNKDLFGKSDPYLEFHQTSDGNWLMVHR
 TEVVKNLNPVWRPFKISLNSLCYGDMDKTIKVECYDYDNDGSHDLIGTFQTTMTKLKE
 ASRSPVEFECINEKKRQKKSYKNSGVISVKQCEITVECTFLDYIMGGCQLNFTVGVD
 TGSNGDPRSPDSLHYISPNGVNEYLTALWSVGLVIQDYDADKMFPAGFGAQIPPPQWQ
 VSHEFPMFNPNPSNPYCNGIQGIVEAYRSCLPQIKLYGPTNFSPINHVARFAAAATQQQT
 ASQYFVLLIITDGVITLDLDETRQAIVNASRLPMSIIIVGVGGADFSAMEFLGDGGSLRSPL
 GEVAIRDIVQFVPFRQFQNAPKEALAQCVAEIPQQVVGYFNTYKLLPPKNPATKQQKQ

SEQ ID No:242

RHTRTHRDTRHETYTHAHTDAHTCTHMHRDTQMHTHTICRKKYALTNIQAAMGLSDPAA
 QPLLGNGSANIQLVKNGENQLRKAEEQGQQDPNKNLSPTAVINITSEKLEGKEPHPQDS
 SSCEILPSQPRRTKSFLNYYADLETSARELEQNRGNHHGTAEEKSQPVQQQASTIING
 DLLLQKPNRPQSSPEDGQVATVSSPETKKDHPKTGAKTDCALHRIQNLAPSDEESSW
 TTLSQDSASPSSPDETDIWSDHSDQTDPPGKRVSDIAGTYWHIPTGTTQWERP
 VSIPADLQGSRKGSLSVTPSPTPENEKQPWSDFAVLNGGKINSIDIWKLHAATVNPDP
 SLKEFEGATLRYASLKLRNAPHPDSSCSINSDPEAKCFAVRSLGWVEMAEDLAPG
 KSSVAVNNCIRQLSYCKNDIRDTVGIWGEKGKDMYLILENDMLSLVDPMDRSVWHSQPIV
 SIRVGVGRDNGRDFAYVARDKDTRILKCHVFRCDTPAKAIATSLHEICSKIMAERKNAK
 ALACSSLQERANVNLDVPLQVDFPTPKTELVQKFHVQYLGMLPVDPVGMIDILNSAIEN
 LMTSSNKEDWLSVNMNVADATTVISEKNEEEVLVECRVRFLSFMSGVGKDVHTFAFIM
 DTGNQRFECHFWCEPNAGNVSEAVQAACMLRYQKCLVARPPSQKVRPPPPPADS
 TRRVTTNVKRGVLSLIDLKQKRPVTEMP

SEQ ID No:243

MSGFSPELIDYLEGKISFEEFERRREERKTREKKSLQEKGKLSAENPDDSEVPSSSGIN
 NSTKSQDKDVNEGETSDGVRKSVHKVFASMLGENEDDEEEEEEEEEETPEQP
 TAGDVFVLEMVLNRETKKMMKEKRPRSKLPRALRGLMGEANIRFARGEREELMCMEI
 IRQAPLAYEPFSTLAMIYEDQGDMEKSLQFELIAAHLNPSDTEEWVRLAEMSLEQDNIKQ
 AIFCYTKALKYEPTNRYLWERSSLYEQMGDHKMAMDGYRRILNLSPSDGERFMQLA
 RDMAKSYYEANDVTSAINIIDEAFSKHQGLVSMEDVNIAAELYISNKQYDKALEIITDFSGI
 VLEKKTSEEGTSEENKAPENVCTIPDGVPIDITVKLMVCLVHLNILEPLNPPLLTLVEQN
 PEDMGDLYLDVAEAFLDVGEYNALPLLSALVCSEYNLAVVWLRHAECLKALGYMER
 AAESYGKVVDLAPLHLDARISLSTLQQQLGQPEKALEALEPMYDPDTLAQDANAQQEL
 KLLLHRSTLLFSQGKMYGYVDTLLTMLAMLLKVAMNRAQVCLISSSKSGERHYLIKVSR
 DKISDSNDQESANCDAKAIFAVLTSVLTKDDWWNLLLKAIYSLCDLSRFQEAELLVDSSL
 EYYSFYDDRQKRKELEYFGLSAAILDKNFRKAYNYIRIMVMENVNPKQLWNIFNQVTMH
 SQDVRHHRFCLRLMLKNPENHALCVLNGHNAFSGSFKHAGQYVQAFRTHPDEPLY
 SFCIGLTFIHMASQKYVLRRHALIVQGFSFLNRYLSLRGPCQESFYNLGRGLHQLGLIHL
 AIHYYQKALELPPLVVEGIELDQLDLRRDIAYNLSLIYQSSGNTGMAQTLLTYCSI

SEQ ID No:244

MLRRVTAAVCATRRKLCEAGRELAALWGIETRGRCEDSAAARPFPILAMPGRNKA
 TCSCPDLPNGQDLGENSRVARLGADEEEEEGRGSLSNAGDPEIVKSPSDPKQYRYI
 KLQNGLQALLISDLSNMEGKTGNTTDEEEEEEVAAAALCVGVGSFADPDDLPGLAH
 DEFDDDEHDDDLTDNELEELEERAEARKKTTEKQSAAALCVGVGSFADPDDLPGLAH
 FLEHMVFMGSLKYPDENGFDAFLKKHGGSDNASTDCERTVFQFDVQRKYFKEALDRW
 AQFFIHPLMIRDAIDREVEAVDSEYQLARP
 SDANRKEMLFGLARPGHPMGKFFWGNA
 ETLKHEPRKNNIDTHARLREFWMRYYSSHMTLVVQSKETLDTLEKWVTEIFSQIPNNG
 LPRPNFGHLDLDPFDTPAFNKL
 YRVVPIRKIHALTITWALPPQQQHYRVKPLHYISWLVGH
 EGKGSILSFLRKKCWALALFGGNGETGFEQN
 STYSVFSISITLTDEGYEHFYEVAYTVFQ
 YLKMLQKLGPEKRIFEEIRKIEDNEFHYQE
 QTDPVEYVENMCENMQLYPLQDILTGDQ
 FEYKPEVIGEALNQLVPQKANLV
 LLSGANEGKCDLKEKWFGTQYSIEDIENS
 WGE
 LWNS
 NFELNPDLHLPAENKYIATDFTL
 KA
 FDCPETEY
 PVKIV
 NTPQGCLWY
 KKDNKF
 KIPKAYIR
 FHLISPLIQ
 KSAANV
 VLF
 DIFVN
 ILTHN
 LAEP
 PAYE
 ADVA
 QLEY
 KLV
 AGE
 HGLI
 IRV
 KG
 FN
 HK
 LPLLFQLIIDY
 LAEFN
 STPAV
 FT
 MITE
 QLK
 KTY
 FN
 ILIK
 PET
 LA
 KV
 DV
 RLL
 ILEY
 ARWS
 MIDKY
 QALMDGLS
 LESLLSFV
 KEFKSQLF
 VEG
 LV
 QGN
 VT
 STE
 SMD
 FLKY
 VV
 DV
 KLN
 FK
 PLE
 QEMP

VQFQVVELPSGHHLCKVKALNKGKDANSEVTVYYQSGTRSLREYTLMELLVMHMEEP
 DFLRTKQTLGYHVYPTCRNTSGILGFSVTVGTQATKYNSEVVVDKKIEEFLSSFEEKIENL
 TEEAFNTQVTALIKLKECEDTHLGEEVDRNWNEVVTQQYLFDRLAHEIEALKSFSKSDLV
 NWFKAHRGPGSKMLSVHAVGYGKYELEEDGTPSSEDNSSCEVMQLTYLPTSPLLAS
 VSSPLLISGLSQQHSTFSPTIK

SEQ ID No:245

MAEVGEIIEGCRLPVLRNNQDNEDEWPLAEILSVKDISGRKLFYVHYIDFNKRLDEWVTH
 ERLDLKKIQFPKKEAKTPTKNGLPGSRPGSPEREVPASAQASGKTLPIPVQITLRFNLPK
 EREAIPGGEPDQPLSSSSCLQPNHRSTKRKVEVVSPATPVPSETAPASVFPQNAGARR
 AVAAQPGRKRKSNCGLTDEDSQDSSDGIPSAPRMTGSLVSDRSRHDDIVTRMKNIECIEL
 GRHRLKPWYFSPYPQELTLPVLYLCEFCLKYGRSLKCLQRHLTKCDLRHPPGNEIYRK
 GTISFFEIDGRKNKSYSQNLCLLAKCFLDHKTLYYDTPFLFYVMTEYDCKGFHIVGYFS
 KEKESTEDYNVACILTLPYQRRGYRKLLIEFSYELSKVEGKTGTPEKPLSDLGLLSYRS
 YWSQTILEILMGLKSESGERPQITINEISEITSIKKEDVISTLQYLNLINYYKGQYILTLSEDI
 VDGHERAMLKRLRIDSKCLHFTPDKDWSKRGKW

SEQ ID No:246

MASGRDERPPWRLGRLLLLMCLLLGSSARAHHKAEATTTTSAGAEAAEGQFDY
 YHEEELESALREAAAAGLPGLARLFSIGRSVEGRPLWVRLTAGLGSLIPEGDAGPDAA
 GPDAAGPLLPGRPQVKLVGNMHGDETCSRQVLIYLARELAAGYRRGDPRLVRLNTTD
 VYLLPSLNPDGFERAREGDCGFGDGGPSGASGRDNSRGRDLNRSFPDQFSTGEPPAL
 DEVPEVRALIEWIRRNFVLSGNLHGGSVVASYPFDDSPEHKATGIYSKTSDEVFKYL
 AKAYASNHPIMKTGEPHCPGDEDETFKDGITNGAHWDVEGGMQDNYWANCFEIT
 LELSCCKYPPASQLRQEENNRESLITLIEKVHIGVKGFVKDSITGSGLENATISVAGINH
 NITTGRGDFYRLLVPGTYNLTVVLTGYMPLTVTNVVVKEGPATEVDFSLRPTVTSVIPD
 TTEAVSTASTVAIPNILSGTSSSYQPIQPKDFHHHFDPMEIFLRRFANEYPNITRLYSLG
 KSVESRELYVMEISDNPGVHEPGEPEFKYIGNMHGNEVVGRELLNLIEYLCKNFGTDP
 EVTDLVHNTRIHLMPSMNPDGYEKSQEGDSISVIGRNNNSNNFDLNRNFPDQFVQITDPT
 QPETIAVMSWMKSYPFVLSANLHGGSLVVNYPFDDDEQGLATYSKSPDDAVFQQIALS
 YSKENSQMFQGRPCKNMYPNEYFPHGITNGASWYNPGGMQDWNYLQTNCFEVTEL
 GCVKYPLEKELPNFWEQNRRSLIQFMKQVHQGVRGFVLDA TDGRGILNATISVAEINHP
 VTTYKTGDYWRLLVPGTYKITASARGYNPVTKNVTVKSEGAIQVNFTLVRSSSTDNNES
 KKGKGASSSTNDASVPTTKEFETLIKDLAENGLESMLRSSSNLALALYRYHSYKDLSE

FLRGLVMNYPHITNLGQSTEYRHIWSLEISNKPNVSEPEEPKIRFVAGIHGNAPVGT
 ELLLALAEFLCLNYKKNPAVTQLVDRTRIVIVPSLNPDGRERAQEKDCTSFIGQTNARGK
 DLDTDFTNNASQPETKAIENLIQKQDFSLVALDGGSMLVTYPYDKPVQTVENKETLKH
 LASLYANNHPSMHHMGQPSCPNSDENIPGGVMRGAEWHSHLGSMKDYSVTYGHCP
 TVYTSCCYFPSAARLPSLWADNKRSLLSMLVEVKGVHGFVKDKTGKPIASKAVIVLNEGI
 KVQTKEGGYFHVLLAPGVHNIIIAIDGYQQQHSQVFVHDAASSVVIVFDTDNRIFGLPR
 ELVVTSGATMSALILTACIWCICSIKSNRHKDGFHRLRQHHDEYEDEIRMMSTGSKKS
 LLSHEFQDETDTTEEETLYSSKH

SEQ ID No:247

MASLYQRFTGKINTSRSPAPPEASHLLGGQGPEEDGGAGAKPLGPRAQAAAPRERG
 GGGGGAGGRPRFQYQGRSDGDEEDELVGSNPPQRNWKGIAIAALLVILVICSLIVTSILL
 TPAEDNSLSQKKVTVEDLFSEDFKIHDPEAKWISDTEFIYREQKGTVRLWNVETNTST
 VIEGKKIESLRAIRYEISPDREYALFSYNVEPIYQHSYTGYVLSKIPHGDPSLDPP
 NAKLQYAGWGPKGQQQLIFIFENNYYCAHVGKQAIRVVSTGKEGVIYNGLSDWL
 KTHIAHWSPDGTRLAYAINDSRVPIMELPTYTGSIYPTVKPYHYPKAGSENPSISLHVI
 GLNGPTHDLEMMPDPDMREYYITMVKWATSTKAVTWLNRAQNVSLLCDATTGV
 CTKKHEDESEAWLHRQNEEPVFSKDGRKFFFIRAIHQGGRGKFYHITVSSSQPNSSND
 NIQSITSGDWDTKILAYDEKGKNIYFLSTEDLPRRRQLYSANTEGNFRQCLSDLVEN
 CTYFSASFHSMDFFLKCEGPGVPMVTVHNTTDKKMFDETN
 NEHVKKAINDRQMPK
 VEYRDIEIDDYNLPMQILKPATFTDTTHYPLLVDGTPGSQSVAEKFEVSWETVMVSSH
 GAVVVKCDGRGSGFQGTKLLHEVRRRLGLLEEKDQMEA
 VRTMLKEQYIDRTRAVFG
 KDYGGYLSTYILPAKGENQGQTF
 CGSALSPITDFKLYASAFSERYLGLHGLDNRAYEM
 TKVAHRVSALEEEQQFLIIHPTADEKIH
 FQHTAELITQLIRGKANYSLQIYPDESHYFTSSL
 KQHLYRSIINFFVECFRIQDKLPTVTAKEDEEED

SEQ ID No:248

IQTSGACRARSGGGRDRGCTGRGCGADARAGAACMVKISFQPAVAGIKGDKADKASAS
 APAPASATEILLTPAREEQPPQHRSKRGGSGVGGVCYLSMGMVLLMGLVFASVYIYRF
 FLAQLARDNFFRCGVLYEDSLSSQVRTQMELEEDVKIYLDENYERINV
 VPVQFGGGDPA
 DIIHDFQRGLTAYHDISLDKCYVIELNTIVLPPRNFWELL
 MNVKRGTYLPQTYIIQEEMVV
 TEHVS
 DKEALGSFIYHLCNGKDTYRLRRRATRRRINKRGAKNCNAIRHFENTFV
 VETLIC
 GVV

SEQ ID No:249

MVKVTFNSALAQKEAKKDEPKSGEEALIIPPDAVAVDCKDPDDVVPGQRRAWCWM
CFGЛАFMLAGVILGGAYLYKYFALQPDDVYYCGIKYIKDDVILNEPSADAPAALYQTIEEN
IKIFEEEVEFISVPVPEFADSDPANIVHDFNKKLTAYLDLNLDKCYVIPLNTSIVMPPRNL
LELLINIKAGTYLPQSYLIHEHMVITDRIENIDHLGFFIYRLCHDKETYKLQRRETIKGIQKR
EASNCFAIRHFENKFAVETLICS

29. Jan. 2004

CLAIMS

1. A protein complex selected from complex (I) and comprising
 - (a) at least one first protein, which first protein is selected from the group of proteins in table 1, fourth column of a given complex, or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of said protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions; and
 - (b) at least one second protein, which second protein is selected from the group of proteins in table 1, fifth column of said given complex, or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of said second protein, said variant being encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions; and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4) 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.
2. A protein complex comprising a first protein selected from the proteins listed in table 1, fourth column of a given complex or a homologue or variant thereof, or a functionally active fragment or functionally active derivative of said first protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said first protein under low stringency conditions, and at least one second protein selected from the group of proteins in table 1, fifth column of a given complex, or a variant or homologue thereof, or a functionally active fragment or a functionally active derivative of said second protein, the variant of said second protein being encoded by a nucleic acid that hybridizes to the nucleic acid of said second protein under low-stringency conditions, and wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% BSA, 100 ug/ml denatured salmon sperm

DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4) 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

3. A protein complex comprising all proteins selected from the proteins in table 1, third column of a given complex or at least one protein being a homologue thereof, or a variant thereof or functionally active fragment or functionally active derivative of said protein, said variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said protein under low stringency conditions; wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.
4. A protein complex that comprises all proteins as listed in table 1, third column for a given complex or at least one protein being a homologue or a variant thereof, or a functionally active fragment or a functionally active derivative thereof, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of any of said proteins under low stringency conditions, except at least one protein of the proteins listed in table 5, third column, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C, with the proviso that the complex comprises at least one protein selected from table 1, fifth column of a given complex.

5. The complex of any of Claim 1 - 4 comprising at least one functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein.
6. The complex of Claim 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.
7. The complex of any of Claim 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.
8. The complex of any of Claim 1 - 7 that is involved in at least one biochemical activity as stated in table 3.
9. A process for preparing a complex of any of Claim 1 - 8 and optionally the components thereof comprising the following steps:
expressing a protein of the complex, preferably a tagged protein, in a target cell, or a tissue or an organ, isolating the protein complex which is attached to the protein, preferably the tagged protein, and optionally disassociating the protein complex and isolating the individual complex members.
10. The process according to Claim 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.
11. The process according to any of Claim 9 - 10 wherein the two tags are separated by a cleavage site for a protease.
12. Component of a protein complex obtainable by a process according to any of Claim 9 - 11.
13. Protein selected from the group of proteins in table 1, sixth column of a given complex or a homologue or a variant of thereof, or a functionally active fragment or a

functionally active derivative of said protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

14. Nucleic acid encoding a protein according to Claim 13.

15. Construct, preferably a vector construct, comprising

- (a) a nucleic acid according to Claim 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or
- (b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative thereof, or a homologue or a variant thereof, at least one of said proteins being selected from the first group of proteins according to Claim 1 (a) and at least one of said proteins, being selected from the second group of proteins according to Claim 1 (b) or
- (c) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative thereof, or a homologue or a variant thereof, said proteins being selected from the proteins of complex (II) according to Claim 1.

16. Host cell, containing a vector comprising at least one nucleic acid of Claim 14 and /or a construct of Claim 15 or containing several vectors each comprising at least one nucleic acid encoding at least one protein selected from the first group of proteins according to Claim 1 (a) and at least one nucleic acid encoding at least one protein selected from the second group of proteins according to Claim 1 (b).

17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of

Claim 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody containing the binding domain thereof which binds to any of the proteins of the group of proteins according to Claim 13.

18. A kit comprising in one or more containers:

- (a) the complex of any of Claim 1 – 8 and/or the proteins of Claim 13 and/or
- (b) an antibody according to Claim 17 and/or
- (c) a nucleic acid encoding a protein of the complex of any of Claim 1 – 8 and/or a protein of Claim 13 and/or
- (d) cells expressing the complex of any of Claim 1 – 8 and/or a protein of Claim 13 and, optionally,
- (e) further components such as reagents, buffers and working instructions.

19. The kit according to Claim 18 for processing a substrate of a complex of any one of Claim 1 - 8.

20. The kit according to Claim 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as those as stated in column 2, table 4 of a given complex.

21. Array, preferably a microarray, in which at least a complex according to any of Claim 1 - 8 and/or at least one protein according to Claim 13 and/or at least one antibody according to Claim 17 is attached to a solid carrier.

22. A process for modifying a substrate of a complex of any one of Claim 1 - 8 comprising the step of bringing into contact a complex of any of Claim 1 - 8 with said substrate, such that said substrate is modified.

23. A pharmaceutical composition comprising the protein complex of any of Claim 1 - 8 and/or a protein according to Claim 13.

24. A pharmaceutical composition according to Claim 23 for the treatment of diseases and disorders, preferentially for diseases or disorders such as those as stated in column 2, table 4 of a given complex.
25. A method for screening for a molecule that binds to a complex of any one of Claim 1 - 8 and/or a protein of Claim 13, comprising the following steps:
 - (a) exposing said complex or protein, or a cell or organism containing said complex or said protein, to one or more candidate molecules; and
 - (b) determining whether said candidate molecule is bound to the complex or protein.
26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of a complex of any one of Claim 1 - 8 comprising the steps of:
 - (a) exposing said complex, or a cell or organism containing said complex to one or more candidate molecules; and
 - (b) determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene regulated by the complex and/or the abundance and/or activity of a protein or protein complex dependent upon the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene regulated by the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity, or composition of said complex.
27. The method of Claim 26, wherein the amount of said complex is determined.
28. The method of Claim 26, wherein the activity of said complex is determined.

29. The method of Claim 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.
30. The method of Claim 26, wherein the amount of the individual protein components of said complex is determined.
31. The method of Claim 30, wherein said determining step comprises determining whether any of the proteins listed in table 1, third column of said complex, or a functionally active fragment or a functionally active derivative thereof, or a variant or a homologue thereof, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said protein under low-stringency conditions, is present in the complex.
32. The method of any of Claim 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder, preferentially of a disease or disorder selected from the diseases or disorders such as those as stated in column 2, table 4 of a given complex.
33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of Claim 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder, preferentially of a disease or disorder such as those as stated in column 2, table 4 of a given complex.
34. A method for the production of a pharmaceutical composition comprising carrying out the method of Claim 26 - 31 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, component disposition of, or intracellular localization of the complex of any one of the Claim 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene regulated by the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in a corresponding sample from a subject not having the disease or disorder or predisposition indicated the presence in the subject of the disease or disorder or predisposition in the subject.
36. The method of Claim 35, wherein the amount of said complex is determined.
37. The method of Claim 35, wherein the activity of said complex is determined.
38. The method of Claim 37, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.
39. The method of Claim 35, wherein the amount of the individual protein components of said complex is determined.
40. The method of Claim 39, wherein said determining step comprises determining whether any of the proteins according to Claim 13 is present in the complex.
41. The complex of any one of Claim 1 - 8, or a protein of Claim 13 or an antibody or fragment thereof of Claim 17, for use in a method of diagnosing a disease or disorder, preferentially of a disease or disorder such as neurodegenerative disease such as those as stated in column 2, table 4 of a given complex.

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity of, component composition of or intracellular localization of, the complex of any one of Claim 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, activity of, or protein composition of, said complex.
43. The method according to Claim 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.
44. The method according to Claim 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.
45. Complex of Claim 1 - 8 and/or a protein as listed in table 1, fifth column of said complex as a target for an active agent of a pharmaceutical, preferably a drug target, in the treatment or prevention of a disease or disorder, preferentially of a disease or disorder such as a neurodegenerative disease such as those as stated in column 2, table 4 of a given complex.

